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WITHDRAWN

ORGANIC DERIVATIVES OF ANTIMONY

BY
WALTER G. CHRISTIANSEN
Instructor in the Harvard Medical School

American Chemical Society
Monograph Series

BOOK DEPARTMENT

The CHEMICAL CATALOG COMPANY, *Inc.*
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GENERAL INTRODUCTION

American Chemical Society Series of Scientific and Technologic Monographs

By arrangement with the Interallied Conference of Pure and Applied Chemistry, which met in London and Brussels in July, 1919, the American Chemical Society was to undertake the production and publication of Scientific and Technologic Monographs on chemical subjects. At the same time it was agreed that the National Research Council, in coöperation with the American Chemical Society and the American Physical Society, should undertake the production and publication of Critical Tables of Chemical and Physical Constants. The American Chemical Society and the National Research Council mutually agreed to care for these two fields of chemical development. The American Chemical Society named as Trustees, to make the necessary arrangements for the publication of the monographs, Charles L. Parsons, Secretary of the American Chemical Society, Washington, D. C.; John E. Teeple, Treasurer of the American Chemical Society, New York City; and Professor Gellert Alleman of Swarthmore College. The Trustees have arranged for the publication of the American Chemical Society series of (a) Scientific and (b) Technologic Monographs by the Chemical Catalog Company of New York City.

The Council, acting through the Committee on National Policy of the American Chemical Society, appointed the editors, named at the close of this introduction, to have charge of securing authors, and of considering critically the manuscripts prepared. The editors of each series will endeavor to select topics which are of current interest and authors who are recognized as authorities in their respective fields. The list of monographs thus far secured appears in the publisher's own announcement elsewhere in this volume.

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The development of knowledge in all branches of science, and especially in chemistry, has been so rapid during the last fifty years and the fields covered by this development have been so varied that it is difficult for any individual to keep in touch with the progress in branches of science outside his own specialty. In spite of the facilities for the examination of the literature given by Chemical Abstracts and such compendia as Beilstein's Handbuch der Organischen Chemie, Richter's Lexikon, Ostwald's Lehrbuch der Allgemeinen Chemie, Abegg's and Gmelin-Kraut's Handbuch der Anorganischen Chemie and the English and French Dictionaries of Chemistry, it often takes a great deal of time to coördinate the knowledge available upon a single topic. Consequently when men who have spent years in the study of important subjects are willing to coördinate their knowledge and present it in concise, readable form, they perform a service of the highest value to their fellow chemists.

It was with a clear recognition of the usefulness of reviews of this character that a Committee of the American Chemical Society recommended the publication of the two series of monographs under the auspices of the Society.

Two rather distinct purposes are to be served by these monographs. The first purpose, whose fulfilment will probably render to chemists in general the most important service, is to present the knowledge available upon the chosen topic in a readable form, intelligible to those whose activities may be along a wholly different line. Many chemists fail to realize how closely their investigations may be connected with other work which on the surface appears far afield from their own. These monographs will enable such men to form closer contact with the work of chemists in other lines of research. The second purpose is to promote research in the branch of science covered by the monograph, by furnishing a well digested survey of the progress already made in that field and by pointing out directions in which investigation needs to be extended. To facilitate the attainment of this purpose, it is intended to include extended references to the literature, which will enable anyone interested to follow up the subject in more detail. If the literature is so voluminous that a complete bibliography is impracticable, a critical selection will be made of those papers which are most important.

The publication of these books marks a distinct departure in the policy of the American Chemical Society inasmuch as it is a serious attempt to found an American chemical literature without primary regard to commercial considerations. The success of the venture will depend in large part upon the measure of coöperation which can be secured in the preparation of books dealing adequately with topics of general interest; it is earnestly hoped, therefore, that every member of the various organizations in the chemical and allied industries will recognize the importance of the enterprise and take sufficient interest to justify it.

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To
ELMER PETER KOHLER

Preface.

The chemistry of organo-metallic compounds has been expanding very rapidly during the last few decades, owing largely to the marked physiological activity of these substances. In this great class of compounds, there are, on the one hand, some of the most powerful of the war gases and, on the other hand, some drugs which are indispensable to modern medicine. Although the organic arsenicals have been investigated much more thoroughly than the antimonials, studies in the latter field are being carried on quite actively in connection with researches on protozoal diseases, because it appears that in certain of these diseases the antimonials are much more efficacious than the arsenicals. Throughout the literature there are numerous papers in which these compounds are discussed, but there is no comprehensive compilation of these results to which one may turn. The purpose of this volume is to correlate these widely scattered data in such a way that they will be suitable both for those desiring a general knowledge of the organic derivatives of antimony and for those embarking on researches in this field. To this end the material has been so arranged that the first chapters are devoted to general discussions without the introduction of detailed directions for the production of the various compounds; the latter type of information has been grouped in the last chapters. It is hoped that by impressing the need of extensive study in this branch of chemotherapy that more investigators will undertake the development of antimonials for use in pharmacology.

Even though the antimonyl derivatives of organic compounds cannot be classed as organic antimonials in the strict sense of the words, a consideration of these substances could hardly be omitted because of their importance in the treatment of some tropical diseases and of the fact that in studying the therapeutic value of the new, truly organic antimonials the object is to develop compounds which are more effective than the antimonyls. Also, the ability of organic compounds to form antimonyl derivatives is dependent upon the existence in the molecule of certain arrangements of groups.

The preparation of this monograph was undertaken in connection with a study of antimonials which is being made in the Departments of Pharmacology and of Tropical Medicine at the Harvard Medical School. The expenses necessary for the pursuance of these investigations are being met from a fund for research in the Department of Tropical Medicine, donated by a citizen of Boston.

I wish to acknowledge my indebtedness to Dr. George C. Shattuck for his kindness in contributing a chapter on "Antimonials as Therapeutic Agents" and to Professors Reid Hunt, E. P. Kohler, and James B. Conant for reading and criticizing the manuscript.

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[June 23, 1924.]
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PART I

Chapter 1.

Introduction and Historical Outline.

Although trypanosomiasis, in its many forms, is not encountered with great frequency in temperate regions, it is widely and thickly spread in many parts of the tropics, and in addition to exacting a heavy toll of human life, it also causes great economic losses to these localities by the destruction of large numbers of cattle and horses. The control and elimination of diseases caused by trypanosomes is, therefore, one of the great problems confronting the medical sciences. Progress in this direction is gradually being made, but as yet no substance or group of substances has been discovered whereby an absolute cure for these infections can be attained. In some instances the patients appear to have been permanently cured, but in a large number the disease reappears after treatment. By the application of certain methods of medication persons afflicted with these infections can be maintained in such a condition that they are able to carry on their ordinary duties of life even though they have not been definitely freed from the disease. An example of this is to be found in one of the tropical countries where at one time it was customary to segregate those people who were found to be victims of trypanosomiasis and treat them medically so that, while not permanently cured, many were outwardly fit and able to follow their normal mode of living.

Much of the success that has been attained in recent years in the treatment of trypanosomiasis with antimonials may be attributed to the discovery by Plimmer and Thomsen[1] that the injection of tartar emetic or the analogous sodium salt into mice and rats which were highly infected with trypanosomiasis caused the parasites to disappear with great rapidity from the peripheral blood. This important work was undertaken at the suggestion of Cushny; Mesnil and Nicolle[2] had previously suggested the use of antimony derivatives in trypanosomiasis. Immediately thereafter chemists undertook the production of many new antimonials of both the antimonyl and C-Sb types which have been subjected to therapeutic studies in relation to protozoal infections. Trypanosomiasis is caused by a number of different species of parasites which are apparently very similar morphologically, but which respond somewhat differently to different antimonials. Thus, a compound which is decidedly effective in combating one type of trypanosome may be quite inferior to some other antimonial when applied to a second type. Investigators have devoted themselves to a study of the antimonials particularly because these substances are frequently much more active than the arsenicals in combating certain tropical diseases; in fact, whereas leishmaniasis is hardly affected by arsenicals, very encouraging and successful results have been reported as a result of the use of antimonials. As usual, the results of different investigators do not always agree as to the exact order of efficacy of the various substances which have been examined, but this is to be expected when one considers that the study is still in its infancy and that the field under investigation is very broad.

---

[1] Plimmer and Thomsen: *Proc. Roy. Soc. London,* 80 (B) (1908), 1.

[2] Mesnil and Nicolle: *Ann. Inst. Past.,* 20 (1906), 444.

Although the majority of the researches, both chemical and pharmacological, on antimonials have been prosecuted with the object of developing trypanocidally active substances and are therefore consequences of the discovery made by Plimmer and Thomsen, antimony compounds occupied important positions in medicine and chemistry prior to 1908. The old stories of the perpetual pill, the antimony goblets in which wine was permitted to stand before use, and the extensive use of antimonials in medicine which resulted from "Basil Valentine's" advocacy of its application in a great variety of diseases are too well known to require repetition. It is sufficient to state that the disastrous consequences which followed the promiscuous use of these materials soon impressed upon people in general the toxic nature of antimonials, and the use of such medicants fell into disrepute. It was only as a result of the development of more exact methods of application of these drugs that they resumed an important place in therapy.

The pioneer work on true organic compounds of antimony appeared in the middle of the nineteenth century when the "type theory" was being studied intensively; it was devoted exclusively to the study of aliphatic derivatives. The report of Löwig and Schweizer's [3] investigation of triethylstibine, or stibethyl as they called it, was followed by a rapid succession of papers by Landolt,[4] Löwig,[5] Scheibler,[6] Berlé,[7] Merck,[8] Cramer,[9] and Friedländer,[10] in which homologues of the above compound were discussed. These early researches were devoted solely to the preparation of tri-methyl, ethyl, and amyl stibines by the action of potassium or sodium alloys of antimony on alkyl halides and to the study of the properties of these substances. A slightly different line of attack was adopted by Hofmann [11] and Buckton [12] who ethylated antimony trichloride by means of zinc diethyl. Buckton was attempting to prepare alkyl antimonials of the type R_4Sb and R_5Sb by the action of zinc dialkyls on trialkylstibinic iodides. Although he considered that his experiments gave slight evidence of the existence of such substances, it seems rather improbable that they were formed. Very shortly thereafter the same investigator [13] found that triethylstibine could also be obtained by treating antimonious chloride with mercury diethyl. Active research on aliphatic stibines ceased about this time and very little work has been done in this field during recent years. Partheil and Mannheim [14] isolated the double salts of tetraethyl and propyl stibonium iodides and mercuric iodide after treating the alkyl iodides with antimony amalgam. An unsuccessful attempt was made by Hantzsch and Hibbert [15] to obtain coördination isomers of the type $(CH_3)_3SbXY$ in which X and Y are negative groups; the failure was due to the fact that pentavalent antimony compounds, unlike the nitrogen analogues, can exist in which two negative groups are bound directly to the antimony atom.

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[3] Löwig and Schweizer: *Ann.*, 75 (1950), 315.

As the above methods of alkylation are both very vigorous reactions and lead only to trialkyl stibines, Auger and Billy [16] sought to obtain the primary stibines by employing a less powerful reagent. When they treated antimonious chloride with a Grignard reagent, ethyl magnesium bromide, a complex reaction mixture resulted from which ethylstibinous iodide was isolated. Subsequently, however, the Grignard reaction was used very successfully for the production of tertiary alkyl stibines.[17] Undoubtedly the meagerness with which aliphatic antimonials have been examined in modern times is due to the fact that these substances are of little value therapeutically as compared with the antimonials of the aromatic series, and as was stated above, nearly all of the research on antimonials during the last two decades has been instigated by the desire to obtain trypanocidally active materials.

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[4] Landolt: *Ann.*, **78** (1851), 91; **84** (1852), 44.
[5] Löwig: *J. prakt. Chem.*, [1] **64** (1855), 415; *Ann.*, **97** (1856), 323.
[6] Scheibler: *J. prakt. Chem.*, [1] **64** (1855), 505.
[7] Berlé: *J. prakt. Chem.*, [1] **65** (1855), 385; *Ann.*, **97** (1856), 316.
[8] Merck: *J. prakt. Chem.*, [1] **66** (1855), 56; *Ann.*, **97** (1856), 332.
[9] Cramer: *Jahr. Fort. Chem.*, (1855), 590.
[10] Friedländer: *J. prakt. Chem.*, [1] **70** (1857), 449.
[11] Hofmann: *Ann.*, **103** (1857), 357.
[12] Buckton: *Quart. J. Chem. Soc.*, **13** (1861), 116.
[13] *Ibid.*, **16** (1866), 22.
[14] Partheil and Mannheim: *J. Chem. Soc. Abst.*, **78** (1900) I, 479.
[15] Hantzsch and Hibbert: *Ber.*, **40** (1907), 1508.
[16] Auger and Billy: *Compt. rend.*, **139** (1904), 599.

The study of aryl stibines, which ultimately led to a very fruitful field of research, had its inception in the splendid investigations of Michaelis and his coworkers on the aryl derivatives of phosphorus, arsenic and antimony. Approximately thirty years after the first alkyl stibine was obtained, Michaelis and Reese [18] found that antimony trichloride and bromo-benzene reacted in the presence of sodium to form triphenylstibine, and that mono and diphenylstibinous halides were produced when this substance was heated with antimony chloride. This has proved to be a general method of preparation and has been used successfully in the production of tolyl,[19] anisyl,[20a] ethoxyphenyl,[20b] and xylyl [21] stibines. Morgan and Vining,[22] while studying the large scale production of phenylarsines for use as war gases, developed the technique used in this reaction so that the phenylstibines could be obtained readily in large quantities also. The conversion of the tertiary stibines into primary and secondary stibinous chlorides by heating with antimony trichloride in a sealed tube has been the subject of numerous researches and discussions owing to the contradictory results obtained by different investigators.[23] In the early work [23a,b,c] only one product, either a primary or secondary stibinous chloride, was isolated, whereas in the later studies both were obtained. Morgan and Micklethwait [23d] showed that in the case of triphenylstibine the reaction takes place in two stages, the second of which is reversible. The reversibility of the

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[17] Hibbert: *Ber.*, **39** (1906), 160.
[18] Michaelis and Reese: *Ber.*, **15** (1882), 2877.
[19] Michaelis and Genzken: *Ber.*, **17** (1884), 924.
[20a] Michaelis and Weitz: *Ber.*, **20** (1887), 52.
[20b] Löloff: *Ber.*, **30** (1897), 2835.
[21] Goddard: *J. Chem. Soc.*, **124** (1923), 2315.
[22] Morgan and Vining: *J. Chem. Soc.*, **117** (1920), 777.
[23a] Michaelis and Reese: *Ref.* 18, 17; *Ann.*, **233** (1886), 39.
[b] Hasenbäumer: *Ber.*, **31** (1898), 2910.
[c] Michaelis and Günther: *ibid.*, **44** (1911), 2316.
[d] Morgan and Micklethwait: *J. Chem. Soc.*, **99** (1911), 2286.
[e] May: *ibid.*, **101** (1912), 1033.
[f] Grüttner and Wiernik: *Ber.*, **48** (1915), 1749.

$$2(C_6H_5)_3Sb + SbCl_3 = 3(C_6H_5)_2SbCl$$
$$(C_6H_5)_2SbCl + SbCl_3 \rightleftarrows 2C_6H_5SbCl_2$$

second reaction explains the discrepancies found in the results of the earlier workers. Grüttner and Wiernik [23f] undertook an exhaustive examination of the second stage and showed that, depending upon the procedure employed in isolating the product from the reaction mixture, either the primary or secondary chloride may be obtained. Aryl stibines may also be prepared by treating antimony trichloride with mercury diaryls [23b] or Grignard reagents; [24] in both cases the main product is the tertiary stibine.

The more recent developments in the chemistry of organic antimonials are due to the discovery, made by the Chemische Fabrik von Heyden,[25] that arylstibinic acids may be obtained directly from diazonium compounds by treatment with sodium antimonite. When one considers what an enormous number of primary aromatic antimonials, which could be obtained only with extreme difficulty by the older processes, may readily be prepared by this reaction, the importance of this discovery is apparent. Very little data appeared in the chemical journals regarding this reaction until Schmidt published a very excellent series of papers [26] on the aryl stibinic acids.

Mention should be made of the preparation of compounds in which antimony is attached to an alicyclic ring,[27] tricamphorylstibinic chloride, and heterocylic compounds in which an antimony atom constitutes part of the ring.[28] Compounds of this type, however, have not as yet been found to possess any properties which will make them of great importance.

Inasmuch as the arseno compounds constitute one of the most important classes of organic arsenicals, it is interesting to note that the corresponding stibino compounds [29] (ArSb = SbAr) and the

[24] Pfeiffer and Schnurmann: *Ber.*, **37** (1904), 4620.
[25] Ger. pat.: 254,421 (1912).
[26] Schmidt: *Ann.*, **421** (1920), 174 and following.
[27] Morgan, Micklethwait and Whitby: *J. Chem. Soc.*, **97** (1910), 35.
[28] Grüttner and Wiernik: *Ber.*, **48** (1915), 1473; **49** (1916), 442.
[29a] Ger. pat., 268,451.
[b] Schmidt: *Ann.*, **429** (1922), 149.

arseno-stibino compounds[30] (ArAs = SbAr) have been prepared, and that these substances possess marked trypanocidal activity.

The preparation of antimonyl derivatives of organic compounds dates back many centuries and was originally carried out with tartrates. Although the first description of tartar emetic, potassium antimonyl tartrate, was given by Adrian de Mynsicht in the early part of the seventeenth century, this substance was formed years before, when it was customary to let wine stand in antimony goblets prior to use. At the time the changes which occurred were unknown, but it has since been shown that in the presence of air, aqueous solutions of tartaric acid and its salts slowly dissolve antimony to form antimonyl derivatives[31] with intermediate formation of antimony oxide; in fact, this method has been used to some extent in the large scale manufacture of tartar emetic. The real study of tartar emetic was begun approximately a hundred years ago and has passed through many phases and branched out in many directions. At first the work, which was mainly analytical, contained many contradictions, but in 1842 Dumas and Piria,[32] as a result of carefully conducted experiments, developed the formula $C_{16}H_8O_{10}.Sb_2O_3.KO.H_2O$, or $C_4H_4O_7SbK.1/2H_2O$ as it would be written today, and this has been found to be the correct empirical representation of tartar emetic. These analyses were verified immediately by Berlin,[33] who also examined the extent to which dehydration takes place at various temperatures. As might be expected, these investigators also studied the sodium, ammonium, barium, etc., antimonyl tartrates. Subsequently a great number of salts, especially the substituted ammonium salts resulting from the use of different amines, have been made and studied.[34] It was discovered early in the work that tartaric acid is not the only organic acid which readily yields antimonyl derivatives; in fact, even before the true composition of tartar emetic was known, Thaulow obtained an antimony derivative of

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[30a] Ger. Pat., 269,743; U. S. Pats.: 1,111,821; 1,422,294.
[b] Ehrlich and Karrer: *Ber.*, **46** (1913), 3564.
[31a] Moritz: *Chem. Ztg.*, **26** (1902), 401.
[b] Jordis: *ibid.*, **26** (1902), 632.
[32] Dumas and Piria: *Ann.*, **44** (1842), 85; *Ann. Chim. Phys.*, [3] **5** (1842), 375.
[33] Berlin: *Arch. der Pharm.*, **102** (1847), 259; *Ann.*, **64** (1847), 359.
[34a] Hesse: *Ann.*, **46** (1868), 369.
[b] Clarke: *Ber.*, **15** (1882), 1540.
[c] Grandeau: *Ann. Chim. Phys.*, [3] **67** (1863), 231.
[d] Strömholm: *Ber.*, **33** (1900), 828.
[e] Fargher and Gray: *J. Pharm. and Exp. Therap.*, **18** (1921), 341.
[f] Brahmachari: *Indian J. Med. Res.*, **10** (1922), 492; **11** (1923), 196.

potassium citrate.[35] The formation of antimonyl compounds was later extended so that derivatives were obtained from many organic acids,[36] and it was concluded from this work that only α hydroxy acids are capable of forming these substances. The structural formula of tartar emetic and of antimonyl compounds in general has been a much debated subject,[37] and two types of formulæ have been propounded. The advocates of one type maintain that the antimonyl group is bound to the molecule by the oxygen of the hydroxyl group whereas those advocating the second type believe that it is the oxygen of the carboxyl group which holds the antimonyl group. In spite of forty years of discussion this point has not yet been definitely settled.

. The existence of a class of antimonials in which the antimony atom is united to the organic part of the molecule by a sulfur atom is very interesting; the substances of this type which have been investigated to date are derivatives of thioglycollic acid. Although a comparatively small amount of work has been done in this field,[38] the very favorable results which were recently obtained [39] in the

[35] Thaulow: *Ann.*, **27** (1838), 334.

[36a] Pasteur: *Ann. Chim. Phys.*, [3] **31** (1851), 87.
[b] Klein: *Compt. rend.*, **96** (1883), 1802.
[c] Henderson and Prentice: *J. Chem. Soc.*, **67** (1895), 1030.
[d] Moritz and Schneider: *Zeit. physik. Chem.*, **41** (1902), 129.
[e] Jordis and Meyer: *Zeit. angw. Chem.*, **17** (1904), 169.
[f] Ger. Pat. 263,455.

[37a] Clarke and Stallo: *Amer. Chem. J.*, **2** (1880-1), 319; *Ber.*, **13** (1880), 1787.
[b] Clarke and Evans: *Amer. Chem. J.*, **5** (1883-4), 241; *Ber.*, **16** (1883), 2379.
[c] Jungfleisch: *Bull. soc. chim.*, [2] **40** (1883), 98.
[d] Guntz: *Compt. rend.*, **104** (1887), 699, 850.
[e] Adam: *Compt. rend.*, **118** (1894), 1273; *Bul. soc. chim.*, [3] **11** (1894), 597.
[f] Kahlenberg: *Zeit. physik. Chem.*, **17** (1895), 605.
[g] Ref., 36c.
[h] Henderson, Orr, Whitehead: *J. Chem. Soc.*, **75** (1899), 557.
[i] Baudran: *Ann. Chim. Phys.*, [7] **19** (1900), 536.
[j] Prunier: *Bull. soc. chim.*, [3] **23** (1900), 101.
[k] Jordis: *Zeit. angew. Chem.*, **15** (1902), 909; **17** (1904), 41.
[l] Ref. 36e.
[m] Hale: *J. Amer. Chem. Soc.*, **24** (1902), 828.
[n] Bougalt: *Bull. soc. chim.*, [3] **35** (1906), 338.
[o] Blanchetière: *Ibid.*, [4] **27** (1920), 477.

[38a] Rosenheim and Davidsohn: *Zeit. anorg. Chem.*, **41** (1904), 246.
[b] Klason and Carlson: *Ber.*, **39** (1906), 732.
[c] Ramberg: *Ibid.*, **39** (1906), 1356.
[d] Holmberg: *Zeit. anorg. Chem.*, **56** (1907-8), 385.
[e] Rosenheim: *Ibid.*, **57** (1908), 359.
[f] Rowntree and Abel: *J. Pharm. and Exp. Therap.*, **2** (1910), 101.
[g] Brunner: Arch. Exp. Path. and Pharm., **68** (1912), 186.

[39] Randall: *J. Urology*, **9** (1923), 491.

treatment of "Granuloma inguinale" with these compounds may stimulate further research along this line.

So far in discussing the investigation of antimonials no mention has been made of the researches which have grown out of the use of antimonials in dyeing. When tartar emetic is used to fix tannic acid on the fibres, an antimony derivative of tannic acid is formed which, like the antimonyl compounds, is not strictly an organic antimonial. The formation of such substances is typical of aromatic compounds containing two hydroxyl groups in the ortho positions to each other. Rosing[40] described the compound obtained with pyrogallol, and Causse,[41] Sanin,[42] and Weinland and Scholder[43] have made further investigations in this field.

[40] Rosing: *Compt. rend.,* **46** (1858), 1140.

[41] Causse: *Compt. rend.,* **115** (1892), 507; **125** (1897), 954; *Ann. Chim. Phys.,* [7] **14** (1898), 526.

[42] Sanin: *J. Amer. Chem. Soc. Abst.,* **4** (1910), 1296.

[43] Weinland and Scholder: *Zeit. anorg. Chem.,* **127** (1923), 343.

Chapter 2.

Aliphatic Antimonials.

A. Alkyl Stibines.

The only alkyl stibines which are known are the tri-methyl, ethyl and amyl compounds and a few derivatives of tripropylstibine. However, no attempts to prepare other tertiary alkyl stibines have been recorded, and it is entirely probable that such substances can exist and might be obtained readily if one cared to investigate them.

It should be borne in mind, that it was not until 1894 that Palmer, after it had become an accepted fact that primary and secondary arsines could not exist, isolated dimethylarsine; in 1901 Palmer and Dehn obtained phenylarsine. Therefore, at some future time the primary and secondary stibines may be prepared. Work in this field is more difficult than in case of the arsenicals due to the fact that carbon-antimony bonds are weaker than carbon-arsenic bonds, and the substances are accordingly less stable; some of the solid organic antimonials undergo decomposition gradually even in the dry state.

Preparation.

1. An alloy of antimony and potassium or sodium converts alkyl halides into tertiary stibines.

$$K_3Sb + 3RX \rightarrow 3KX + R_3Sb$$

Owing to the violent character of this reaction and the inflammability of alkyl stibines, it is necessary to mix the alloy with sand and to work in an inert atmosphere with small quantities. Although alkyl chlorides or bromides may be used, it is preferable to employ the iodides; an excess of the alloy is always introduced. In the case of the lower members of this series, the crude products are obtained from the mixture by distillation after the reaction is complete, but in preparing triamylstibine, it is advisable to extract the product with ether because the product undergoes decomposition during distillation. In order to remove any unchanged alkyl halide which, if permitted to remain, would combine with the trialkyl stibine to form a stibonium salt, the material is rectified over fresh potassium-antimony alloy.

2. When antimony amalgam, instead of an antimony-potassium alloy, is heated with an alkyl iodide, the reaction is much less violent, and a quaternary stibonium iodide is obtained in the form of double salt with mercuric iodide. When the double salt is treated with moist silver oxide, a solution of the corresponding quaternary stibonium hydroxide is obtained, and after evaporating to dryness, the residue is heated at 100° in order to convert it into the tertiary stibine.

$$Hg_3Sb_2 + 8RI \rightarrow 2(R_4SbI.HgI_2) + HgI_2$$

3. The stibines may also be prepared indirectly by heating coarsely divided metallic antimony with an alkyl iodide in a sealed tube at 140°. The reaction products are antimony tri-iodide and a trialkylstibinic iodide; the latter, when distilled with zinc, is converted into the tertiary stibine.

$$4Sb + 9RI \rightarrow 3R_3SbI_2 + SbI_3$$
$$R_3SbI_2 + Zn \rightarrow R_3Sb + ZnI_2$$

4. Instead of starting with antimony as such or in the form of an alloy, antimony trichloride may be alkylated by zinc dialkyls; the reaction proceeds very readily and large yields of pure trialkyl stibine are obtained. The zinc dialkyls may be replaced by the corresponding mercury compounds, but whereas both of the alkyl groups of the zinc dialkyl are available for alkylation, only one of those in the mercury dialkyls enters into the reaction; the other remains attached to the mercury and appears in the reaction products as an alkyl mercuric halide. When mercury dimethyl is employed, the reaction is complicated by the tendency of the antimony in the stibine to become pentavalent, thereby producing some metallic mercury and trimethylstibinic chloride. The free stibine may be obtained from the dichloride by distillation with zinc.

$$3ZnR_2 + 2SbCl_3 \rightarrow 2SbR_3 + 3ZnCl_2$$

$$2Hg(CH_3)_2 + SbCl_3 \rightarrow (CH_3)_3SbCl_2 + CH_3HgCl + Hg$$

5. In this series, as in so many others, the zinc alkyls may be replaced by Grignard reagents. When an ethereal solution of an alkyl magnesium halide (3 mol. equiv.) is treated with antimony

trichloride (1 mol. equiv.) a vigorous reaction takes place. Upon subsequent distillation in a stream of carbon dioxide the tertiary stibine volatilizes with the ether and may be isolated from the distillate as such or as a trialkyl stibinic halide. If an excess of antimonious chloride is used, a complex mixture results, which contains little or no trialkyl stibine. A modification of this reaction involves the substitution of an antimony pentachloride for the trichloride. When this is done the antimonial which forms is a trialkyl stibinic halide which may be isolated as the di-iodide.

$$6RMgBr + 2SbCl_3 \rightarrow 2R_3Sb + 3MgCl_2 + 3MgBr_2$$

Of these methods of preparation that in which antimony trichloride is treated with a Grignard reagent appears to be the one which is best suited for the preparation of alkyl stibines. The others are either indirect or involve the use of reagents which are difficult to manipulate.

Properties. The tertiary alkyl stibines are colorless, fuming liquids which are heavier than water and insoluble in water, but soluble in organic solvents. The lower members of the series can be distilled without decomposition, but triamylstibine partly decomposes when distilled at atmospheric pressure. They are all very susceptible to oxidation, and the methyl and ethyl compounds burst into flame spontaneously when exposed to the air in large quantities; the amyl derivative behaves similarly if heated to 80°. The ease of oxidation of the latter compound is evident from the facts that if a drop of the liquid is exposed to the air on a piece of filter paper the heat of oxidation is sufficient to char the paper, and if an ether solution of it is slowly evaporated in the air, the residue is not the stibine but triamylstibinic oxide. The stibines are best preserved under water.

The strong tendency for these compounds to pass into derivatives of pentavalent antimony is shown not only by the ease with which they undergo oxidation but also by the strong affinity which they possess for halogens and sulfur and, as has been found with triethylstibine, for selenium. In each case alkyl stibinic halides or sulfides may be secured by direct addition; as in the case of oxidation, the vigor with which this reaction occurs is greatest with the lower members of the series. Trimethylstibine possesses this property to such a marked degree that, in addition to uniting explosively with halogens, it reduces gold and mercuric chlorides and silver nitrate, thereby precipitating the free metals from the solutions. Other examples of this tendency are: the evolution of hydrogen and the formation of triethylstibinic chloride when the tertiary stibine is treated with concentrated hydrochloric acid; the evolution of lower oxides of nitrogen when triethylstibine dissolves in nitric acid to form the dinitrate, and the production of metallic mercury and trimethylstibinic chloride when antimonious chloride is methylated with mercury dimethyl.

The formation of quaternary stibonium compounds also takes place more readily with the simpler tertiary stibines. Thus, while methyl iodide adds very readily to trimethylstibine with the evolution of heat, ethyl iodide and triethylstibine unite only very slowly at ordinary temperatures but quite vigorously at 100° ; the latter reaction will take place gradually at room temperature in the presence of water, which dissolves the stibonium compound as it forms. Triamylstibine and amyl iodide, however, do not combine even when heated in a sealed tube at 100°. Although methyl iodide adds to triethylstibine more readily than ethyl iodide does, the reaction is much less vigorous than with trimethylstibine.

Crystalline double salts have been obtained by the action of platinum and gold chlorides on triethylstibine, but in view of the reducing action which trimethylstibine exhibits toward gold chloride, it is probable the formation of these double salts is preceded by reduction of the metallic salts to the platinous and aurous stage.

B. Alkyl Stibinic Oxides (R_3SbO) and Their Salts.

Preparation of Oxides.

1. If trialkyl stibines are subjected to oxidation by the air under carefully controlled conditions, it is possible to obtain the corresponding stibinic oxides. With the amylstibine this may be done quite successfully, but in the case of the more reactive methyl compound, the reaction proceeds beyond this point, and the product is contaminated with other oxidation products. More satisfactory results are obtained by the action of mercuric oxide on an alcoholic solution of the stibine; the mercury separates, and a solution of the pure oxide is secured.

2. The stibinic oxides may be prepared very readily from the corresponding salts by double decomposition reactions. Thus, the

stibinic halides, which may be prepared directly from the stibines, yield the oxides when treated with silver oxide, or the sulfates, which may be obtained from the halides by use of silver sulfate, may be converted into the oxides by treatment with barium hydroxide.

Preparation of Salts.

1. Some of these salts, namely the halides and sulfides, may be prepared directly from the tertiary stibines by the addition of halogens or sulfur. Owing to the violence with which this reaction occurs it is desirable to add a diluent.

2. The most general and convenient method of preparation is by neutralization of the oxide with the acid in question.

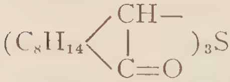
3. One salt may be converted into another by metathesis, e.g.:

$$\begin{gathered} R_3SbS + Hg(CN)_2 \rightarrow \mathit{HgS} + R_3Sb(CN)_2 \\ R_3SbCl_2 + 2AgNO_3 \rightarrow \mathit{2AgCl} + R_3Sb(NO_3)_2 \\ R_3SbSO_4 + BaBr_2 \rightarrow \mathit{BaSO_4} + R_3SbBr_2 \\ R_3SbBr_2 + 2KCNS \rightarrow 2KBr + R_3Sb(CNS)_2 \end{gathered}$$

4. The dihalides may be obtained directly during the preparation of the organic antimonials. When antimony and an alkyl iodide are heated in a sealed tube, a trialkyl stibinic iodide is formed; when a Grignard reagent reacts with antimony pentachloride, a trialkyl stibinic chloride results; and when antimony trichloride reacts with mercury dimethyl, trimethylstibinic chloride is produced.

Properties. The oxides are, with the exception of the crystalline methyl compound, viscous sirups which are soluble in water and alcohol but not in ether. They react with mineral acids to form salts of the types R_3SbCl_2 and R_3SbSO_4. The crystallizing power of the salts, like that of the oxides, decreases as the size of the alkyl group increases. Thus, while the salts derived from trimethylstibine are all crystalline, the chloride and bromide of the ethyl compound are liquids, and the dinitrate is the only crystalline salt of the amyl series. The solubility in water, likewise, decreases with increasing complexity of the alkyl group; even triamylstibinic nitrate is insoluble in water. The salts bear certain resemblances to those of metals, e.g., the sulfides precipitate the sulfides of the heavy metals from solutions of their salts, the cyanides cause the formation of Prussian blue when added to a mixture of ferric and ferrous salts, iodine is liberated from the iodides by the action of chlorine or bromine, many double decomposition reactions with metallic salts are obtained (cf. above), and triethylstibinic oxide precipitates the hydroxides of the heavy metals from solutions of their salts.

The strong affinity for electro-negative elements, and the ability to displace weakly positive metals from their salts and to liberate hydrogen from hydrogen chloride which the tertiary stibines possess are properties commonly associated with fairly strongly electro-positive metals. Also, it would appear from the precipitation of metallic hydroxides by alkyl stibinic oxides and from the behavior of the trialkyl stibinic salts that the oxides are distinctly strong bases. Hantzsch and Hibbert,[1] as a result of an examination of trimethylstibinic oxide and the corresponding bromide, concluded that the base is a decidedly weak one and that the dibromide is hydrolyzed in dilute aqueous solution to $(CH_3)_3SbOHBr$; the latter compound, however, is hydrolyzed only slightly. Conductivity experiments in dilute solutions prepared from the dibromide gave very high values for the molecular conductivity. Moreover, these solutions could be titrated with sodium hydroxide and phenolphthalein just as sharply as solutions of free hydrobromic acid, and the free oxide in the pure state was found to be neutral to litmus. It, therefore, seems necessary to seek some other explanation of the metalloid characteristics of the tertiary alkyl stibines, and the reactions of the oxides and salts. If the stibines are looked upon as strong reducing agents in which the antimony has a great tendency to pass into the pentavalent condition, their behavior toward strongly negative elements, mercuric and auric chlorides, and hydrochloric and nitric acids can be satisfactorily understood. The stibinic oxides, which in aqueous solution exist as $R_3Sb(OH)_2$, do have some, even though only slight, basic properties because $(CH_3)_3Sb(OH)Br$ is only slightly hydrolyzed even in dilute solution. The apparently strong basic character of the oxides is not, therefore, due to extensive ionization of this substance but to the fact that it is soluble, whereas the hydroxides of the heavy metals are not.

As the antimonial which may be obtained from camphor is an alicyclic compound, it may well be mentioned in connection with the aliphatic antimonials. When sodium camphor and antimony trichloride are heated in dry toluene, tricamphorylstibinic chloride[2]—  $\left(C_8H_{14}\left\langle\begin{array}{l}CH-\\ |\\ C=O\end{array}\right.\right)_3SbCl_2$—is obtained. This substance is quite stable toward acids but is readily hydrolyzed by alkalies into antimonic acid and camphor.

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[1] Hantzsch and Hibbert: *Ber.*, **40** (1907), 1508.

[2] Morgan, Micklethwait, and Whitby: *J. Chem. Soc.*, **97** (1910), 35.

C. Quaternary Stibonium Compounds.

Preparation. 1. Tetra-alkyl stibonium iodides are obtained by the addition of alkyl iodides to tertiary stibines; this occurs exothermically at room temperature in the methyl series, only after warming in the ethyl series, but not at all even at 100° in the amyl series. Mixed alkyl stibonium salts, e.g., methyl-triethylstibonium iodide can also be readily prepared in this way. From the iodides, the hydroxides may be secured very easily by the action of moist silver oxide. Once the hydroxides have been obtained, innumerable salts, not only of mineral acids but of organic acids as well, may be prepared by the process of neutralization. Also, one salt may be converted into another by the usual metathetical reactions, e.g.,

$$(R_4Sb)_2S + CuSO_4 \rightarrow CuS + (R_4Sb)_2SO_4$$

In addition to the neutral salts of dibasic acids, quaternary stibonium acid salts such as $(CH_3)_4SbHSO_4$ exist.

2. The quaternary stibonium iodides are obtained in the form of double salts with mercuric iodide when antimony amalgam and an alkyl iodide are heated at a high temperature under pressure. When the double salt is treated with moist silver oxide, the stibonium hydroxide is secured. Tetrapropylstibonium hydroxide has been prepared by this method.

Properties. The stibonium salts are crystalline substances which are easily soluble in water and which, in some cases, are very hygroscopic. Chemically they are extremely similar to salts of the alkali metals, and all the ionic reactions of potassium salts may be paralleled in this series. Tetramethyl and tetrapropyl stibonium hydroxides are deliquescent solids, but the tetra-ethyl and methyl-triethyl compounds are viscous oils. These hydroxides resemble caustic alkalies very closely, i.e., they absorb carbon dioxide and moisture rapidly from the air, dissolve in water with the evolution of heat to form strongly alkaline solutions, liberate ammonia from ammonium salts, saponify fats, precipitate the hydroxides of the heavy metals[3] from solutions of their salts, and when in excess redissolve zinc, aluminum, and tin hydroxides. Bredig[4] examined the molecular conductivity of solutions of tetramethylstibonium hydroxide and compared it with that of the analogous nitrogen compound; his results are given in Table I.

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[3] Tetramethylstibonium hydroxide even precipitates barium hydroxide from its salts.

[4] Bredig: *Zeit. physik. Chem.*, 13 (1894), 301.

TABLE I

Conductivity of Solutions of $(CH_3)_4SbOH$

	$(CH_3)_4SbOH$	$(CH_3)_4NOH$
v[1]	μ	μ
16	166	205
64	169	211
256	171	213

[1] v is the volume in liters per gram-molecule.

The stibonium salts readily form crystalline double salts with mercuric, gold and platinum salts. Steinkopf and Schwen[5] prepared a double salt of tetraethylstibonium iodide and iodoform by boiling these substances in alcoholic solution; the product decomposes into its constituents when boiled with water.

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[5] Steinkopf and Schwen: *Ber.*, **54B** (1921), 2969.

Chapter 3.

Aromatic Stibines and Their Derivatives.

In the aromatic series there exist in addition to the tertiary stibines both mono and di-aryl stibinous chlorides, $ArSbCl_2$ and Ar_2SbCl, but the stibines corresponding to the chlorides are unknown. The processes by which the aryl stibines are prepared always give the tertiary compounds, and the chlorine derivatives of the primary and secondary stibines have to be prepared indirectly.

A. Tertiary Aryl Stibines Obtained by Introduction of Antimony Directly into the Benzene Nucleus.

Preparation.

1. One of the best methods of obtaining aryl stibines is that of Michaelis and Reese,[1] in which an aromatic halogen compound, preferably a bromide, is treated with antimony trichloride and an excess of sodium in the presence of a solvent such as benzene or xylene. In analogous reactions with phosphorus trichloride ether can be used as a solvent, but in the antimony series the reaction takes place very slowly or not at all in ether solution. In some instances, the reaction commences slowly at room temperature, but once under way it proceeds rapidly and cooling may be necessary in order to control it. The mixture is usually refluxed finally to insure complete reaction. After filtration, the benzene is distilled off, and a residue consisting of the aryl stibine is obtained. The reaction is complicated slightly by the formation of small amounts of di- and tri-arylstibinic

$$3ArBr + SbCl_3 + 6Na \rightarrow Ar_3Sb + 3NaCl + 3NaBr$$

halides, Ar_2SbX_3 and Ar_3SbX_2. The applicability of this method is, of course, limited to those aryl bromides which do not contain groups which are susceptible to the action of metallic sodium or antimony trichloride. If moisture is present the products will also be contaminated by traces of stibinic oxides (Ar_3SbO) due to the action of the caustic soda, which is formed from the water, on the triarylstibinic halide. When the bromotoluenes, or other compounds of which there are several isomers, are used they should be carefully purified first in order to avoid the formation of complex reaction mixtures from which the isolation of pure substances is difficult. Thus, if ortho-bromotoluene, containing a fairly large quantity of the para isomer, serves as the starting material, a mixture probably containing tri-o-tolyl, p-tolyl-di-o-tolyl, o-tolyl-di-p-tolyl, and tri-p-tolyl stibines is formed. If, however, the quantity of p-bromo-toluene present is very small, the only by-product is p-tolyl-di-o-tolylstibine which can be separated from the tri-o-tolylstibine.

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[1] Michaelis and Reese: (a) *Ber.*, **15** (1882), 2877; (b) *Ann.*, **233** (1886), 39.

2. The Grignard reaction gives excellent results in the preparation of tri-aryl stibines. It would seem that the use of less than three equivalents of the magnesium compound per equivalent of antimony trichloride should produce primary or secondary aryl stibinous halides but in all cases the product is mainly the tertiary compound. The yields obtained are usually very good; in fact, in the case of triphenyl-

$$3ArMgX + SbX_3 \rightarrow Ar_3Sb + 3MgX_2$$

stibine it is practically quantitative.[2] Goddard,[3] however, secured better yields of the trixylylstibines by the sodium process. Antimonials which are not strictly of the aromatic type, i.e., compounds like tribenzylstibine in which the antimony is not attached directly to the benzene nucleus, are readily obtained by this method.

Owing to the existence of primary and secondary aryl stibinous chlorides, the preparation of many mixed stibines of the types ArR_2Sb and Ar_2RSb has been accomplished by application of the Grignard reaction. Although mixed stibines of the type $Ar_2Ar'Sb$ should be readily obtainable, they have not, except in the case of p-tolyl-di-o-tolylstibine, been prepared. This mixed tolylstibine was isolated as a by-product during the preparation of tri-o-tolylstibine by the sodium process. In connection with these mixed stibines, the heterocyclic antimonials, which in reality are mixed aryl alkyl stibines, should be mentioned. Thus, phenyl cyclotetramethylene and cyclopentamethylene stibines have been prepared by the action of phenylstibinous chloride on the magnesium derivatives of α, δ dibromobutane and α, ε dibromopentane respectively.

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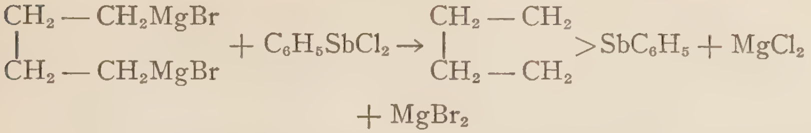
[2] Morgan and Micklethwait: *J. Chem. Soc.*, 99 (1911), 2290.
[3] Goddard: *Ibid.*, 124 (1923), 2315.



$$\begin{array}{l} CH_2-CH_2MgBr \\ | \\ CH_2-CH_2MgBr \end{array} + C_6H_5SbCl_2 \rightarrow \begin{array}{l} CH_2-CH_2 \\ | \\ CH_2-CH_2 \end{array}\!\!>SbC_6H_5 + MgCl_2 + MgBr_2$$

3. The treatment of an organic halide with an alloy of antimony may be employed in the aromatic as well as in the aliphatic series for the preparation of tertiary stibines. In this case, however, the reaction is much less vigorous; it is necessary to reflux sodium antimonide and p-bromoanisole for many hours in order to obtain even a small yield of the tri-anisylstibine. Although this method could be used in many instances, one would not be likely to select it in view of the necessity of preparing sodium antimonide, and the absence of any advantages over either the Grignard process or the sodium method of Michaelis and Reese.

$$3ArBr + Na_3Sb \rightarrow Ar_3Sb + 3NaBr$$

4. The expectation that aryl stibines could be obtained in satisfactory yields by the action of mercury di-aryls on antimonious chloride has not been realized. In numerous experiments, Michaelis and Reese[1] obtained phenylmercuric chloride by treating antimony trichloride both in the molten condition and in the presence of solvents with mercury diphenyl but in no case could they isolate any aryl stibines. After heating these reagents in dry xylene in a sealed tube at 130°, Hasenbäumer[4] was able to isolate triphenylstibinic chloride and small quantities of diphenylstibinic chloride, $(C_6H_5)_2SbCl_3$.

The number of stibines which may be prepared by the above methods is somewhat limited due to the necessity of avoiding the presence, in the benzene ring, of substituents which will either be attacked by the reagents—metallic sodium or antimony trichloride—or interfere with the formation of aryl magnesium halides. Also, the use of dichloro or dibromo benzenes would hardly be feasible due to the presentation of two positions for the antimony to become attached to the ring and thereby tending to increase the complexity of the reaction mixtures which are obtained. For these reasons the only aryl stibines which have been obtained by direct introduction of antimony are triphenylstibine, its homologues, the tolyl and xylyl compounds, and its methoxy and ethoxy substitution products. By various indirect methods other triaryl stibines may be prepared, but

[4] Hasenbäumer: *Ber.*, **31** (1898), 2910.

they may well be reserved for discussion until after the general reactions of the aryl stibines have been described.

Properties. The triaryl stibines are crystalline solids which have definite melting points and which are quite stable in the air. It will be recalled that the metalloid properties of the trialkyl stibines were shown to be consequences of the extreme oxidizability of these substances. The stibines of the aromatic series are also susceptible to oxidizing agents but not to the extent which the alkyl compounds are. Thus, while they combine directly though not violently with halogens to form stibinic halides, they are quite stable with respect to atmospheric oxygen and do not unite directly with sulfur. In fact it was only as a result of the work of Kaufmann[5] that triphenylstibinic sulfide was obtained after Michaelis and Reese had concluded that this substance was non-existent. In some instances, as will be pointed out later, the reaction with halogens is far more complicated than the mere formation of a dihalide. The aryl stibines are sufficiently strong reducing agents to convert cupric, thallic, and ferric chlorides into the corresponding cuprous, thallous, and ferrous chlorides, but they do not reduce any metallic salts to

$$Ar_3Sb + 2CuCl_2 \rightarrow Ar_3SbCl_2 + Cu_2Cl_2$$

such an extent that the free metal precipitates. Oxidation by means of concentrated nitric or sulfuric acids is accompanied by the formation of a triaryl stibinic nitrate or sulfate and the evolution of nitrous gases or sulfur dioxide. Unlike the alkyl analogues, these

$$(C_6H_5)_3Sb + 2H_2SO_4 \rightarrow (C_6H_5)_3SbSO_4 + SO_2 + 2H_2O$$

stibines are unable to reduce the hydrogen of hydrochloric acid to molecular hydrogen with the simultaneous formation of a stibinic chloride. Potassium permanganate, in either acid or alkaline solution, oxidizes these substances to triaryl stibinic oxides or hydrated oxides, i.e., triaryl stibinic hydroxides. A similar result may be attained by oxidation with hydrogen peroxide in neutral solution; in the presence of alkali this reaction will, depending upon the experimental conditions and the nature of the substituents present in the benzene ring, be accompanied by a certain amount of dearylation.[6] Thus, while triphenylstibine in the presence of cold dilute alkali is readily converted into triphenylstibinic hydroxide, oxidation in hot alkali produces sodium diphenylstibinate—$(C_6H_5)_2SbO_2Na$.

[5] Kaufmann: *Ber.*, 41 (1908), 2762.
[6] Schmidt: *Ann.*, 429 (1922), 123.

Also, tri-p-acetylaminophenylstibine is converted quite easily during alkaline oxidation with hydrogen peroxide into sodium di-p-acetylaminophenylstibinate.

$$(p\text{-}CH_3CONHC_6H_4)_3Sb \rightarrow (p\text{-}CH_3CONHC_6H_4)_2SbO_2Na + C_6H_5NHCOCH_3$$

The C-Sb linkage in the tertiary stibines may be ruptured in several ways. It would be expected from the behavior of the triaryl stibines toward cupric, thallic, and ferric chlorides that a similar result would be obtained with mercuric chloride, but this is true only to a slight extent, i.e., triphenylstibine only slightly reduces mercuric chloride to the mercurous stage. The main reaction in the case of triphenylstibine is one in which the C-Sb bond is severed forming phenylmercuric chloride and antimony trichloride. A similar result has been obtained with all the homologues of triphenylstibine except the tri-o-tolyl compound. In the cases of the homologues, however, a double salt of the stibine with the mercuric chloride ($Ar_3Sb \cdot HgCl_2$) may be isolated as an intermediate; when heated these molecular compounds decompose to form an aryl mercuric chloride in which the —HgCl group occupies the position in the benzene ring formerly held by the antimony. This reaction has, therefore, been used to determine the location of the antimony in some of these compounds. It is entirely probable that in the case of the phenyl compound the double salt is also formed as a very unstable intermediate. The double salt obtained from tri-o-tolylstibine is so stable that it remains unchanged even when heated at 250°. Other examples of the severance of this bond are: the decomposition of triphenylstibine by zinc dimethyl at 200° into toluene, antimony, and a little benzene;[7] the conversion of the same stibine into triphenylarsine and antimony upon heating with arsenic;[8] and the deep-seated changes which take place when the tertiary stibines are heated at a high temperature with methyl iodide. Experiments indicate that from triphenylstibine and methyl iodide at 200°—there is no reaction at 170°—trimethylstibinic iodide, ethane, and iodobenzene are formed.[8] None of the strictly aromatic stibines react with alkyl halides forming stibonium compounds.

It will be noticed that the properties which have just been described are only those in which the antimony atom is directly concerned. The reactions which these substances undergo due to the presence in the molecule of an aromatic nucleus will be discussed below in that section which deals with the conversion of one tertiary aryl stibine into another.

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[7] Michaelis and Reese: *Ann.*, 233 (1886), 39.

[8] Morgan, Organic Compounds of Arsenic and Antimony, Longmans (1918), p. 305.

A comparison of the reactions of the aliphatic and aromatic stibines shows that they are essentially of the same type but that in the latter series the susceptibility to oxidation is much less; spontaneous inflammability, violent reactivity with halogens, and reduction of metallic salts to the free metal, are not encountered. Further evidence of the decreased tendency to pass from trivalent to pentavalent antimonials in this series is the non-formation of stibonium compounds when the aryl stibines are heated with methyl iodide. The mixed aryl alkyl stibines should and do occupy intermediate positions between the two types, and the degree to which they resemble one type or the other depends upon the number of aryl and of alkyl groups which are present. Phenyl-cyclopentamethylenestibine, which is also an aryl alkyl stibine, has properties similar to those of the other mixed stibines. The gradation between the two types of stibines is clearly brought out in Table II.

Phenyl-cyclopentamethylenestibine reacts in the same manner as triphenylstibine when treated with mercuric chloride; thus, instead of forming a double compound, it is decomposed. It is understood of course that these mixed stibines also possess the properties which have been found for stibines in general.

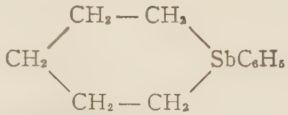
B. Tertiary Aromatic Stibinic Salts.

Preparation.

The halides are the most readily obtainable of the triaryl or aryl alkyl stibinic salts and are usually prepared by adding the halogen to a solution of the stibine in some solvent such as ether, chloroform, carbon tetrachloride, or petroleum ether. The products may crystallize directly or be secured by evaporation of the solvent. In a few instances, such as the preparation of tri-p-anisylstibinic chloride and the analogous ethoxy compound,[9] in which the stibine is very sensitive to chlorine, the salt may be prepared by chlorination with cupric chloride; the cuprous chloride separates and is easily removed from the solution of the dichloride. When tri-p-anisylstibine is chlorinated with free chlorine, besides addition to

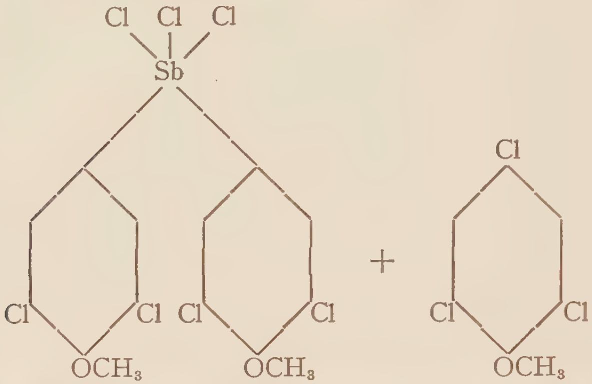
[9] Löloff: *Ber.*, 30 (1897), 2835.

TABLE II.

	Physical State	*Behavior in Air*	*Behavior with CH_3I*
$(CH_3)_3Sb$	Liquid b.p. 80°	Spontaneously inflammable	Forms $(CH_3)_4SbI$ exothermically
$C_6H_5(CH_3)_2Sb$	Liquid b.p. 112°/16-18 mm.	Fumes, oxidizes very readily	Forms $C_6H_5(CH_3)_3SbI$ quite readily at room temperature.
$(C_6H_5)_2CH_3Sb$	Oil—b.p. 174°/16-18 mm.	Oxidizes readily but does not fume	No reaction even at 100°
	Oil—b.p. 169-171°/18-20 mm.	Oxidizes slowly	No reaction even at 100°
$(C_6H_5)_3Sb$	Plates—m.p. 48°	Stable	No reaction even at 170°

the antimony atom, substitution in the benzene ring and fission of one of the C-Sb bonds take place as shown in the equation.

$$(p\text{-}CH_3OC_6H_4)_3Sb + 5Cl_2 \longrightarrow$$



Treatment of a dichloride or bromide with alkali, preferably in alcoholic solution, produces a dihydroxide as such or its dehydration product, a stibinic oxide. These substances may also be secured directly from the stibine by oxidation processes; in the aromatic series it is usually necessary to use some oxidizing agent other than atmospheric oxygen, e.g., potassium permanganate in neutral or alkaline solution or hydrogen peroxide in neutral solution. The oxides and dihydroxides react readily with acids forming salts; in this way they may be converted into the dihalides, dinitrates, sulfates and in isolated cases into di-acetates.[10] The stibinic nitrates and sulfates may also be obtained directly from the stibines by oxidation with concentrated nitric or sulfuric acids; this method might introduce side reactions involving nitration or sulfonation of the benzene nucleus.[11] Another method of production of these salts is by application of double decomposition reactions; tri-p-methoxy or ethoxy phenylstibinic chloride when treated with alcoholic silver nitrate yields the corresponding dinitrate.[9]

The aryl stibinic salts, like the analogous aliphatic compounds are prone to suffer hydrolysis; the presence of moisture in the chloroform used during recrystallization of tri-p-tolylstibinic iodide causes the formation of a small amount of a basic iodide $(p\text{-}CH_3C_6H_4)_3Sb(OH)I$,[12] and during the preparation of triphenylstibinic nitrate from the dichloride and silver nitrate in ordinary alcoholic solutions, some hydrolysis occurs producing a small amount of basic nitrate.[13] The hydrolysis of triphenylstibinic sulfate, chloride, and nitrate by boiling in aqueous solution results in the complete removal of one of the negative groups; the basic salts formed in this way are stable and do not undergo further hydrolysis.[13]

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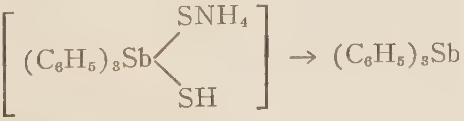
[10] Ref. 3, p. 2322.

[11] These processes will be discussed later.

[12] Michaelis and Genzken: *Ann.*, 242 (1887), 164.

The sulfides of this series were unknown for a long while and were considered to be incapable of existence. The triaryl stibines could not be made to unite with sulfur, and the introduction of hydrogen sulfide into ammoniacal alcoholic solutions of the stibinic chlorides caused the formation of the free tertiary stibine instead of the expected sulfide. This process was used in a number of cases as a method of purifying the stibine. Kaufmann[14] studied this reaction very carefully in the case of triphenylstibine and showed that the sulfide is formed and can be isolated in a yield of 80%; the difficulties encountered in the previous attempts resulted from excessive treatment with hydrogen sulfide. An ammoniacal alcoholic solution of the dichloride contains triphenylstibinic hydroxide, and when hydrogen sulfide is introduced, a precipitate forms which, with continued introduction of hydrogen sulfide, redissolves to form a yellow solution. In the early work on this reaction, the precipitate was considered to be sulfur which redissolved to form ammonium polysulfides. All attempts to isolate a stibinic sulfide from this yellow solution yielded only triphenylstibine and sulfur. Kaufmann showed that the initial precipitate is triphenylstibinic sulfide, and that it dissolves in the ammonium sulfide to form a complex organic antimony sulfide which is very unstable and readily decomposes forming triphenylstibine. The mechanism by which the triphenylstibinic chloride is converted by hydrogen sulfide into the stibinic sulfide and then into the stibine is given as follows:—

$$(C_6H_5)_3SbCl_2 \rightarrow (C_6H_5)_3Sb(OH)_2 \rightarrow (C_6H_5)_3SbS \rightarrow$$



$$\left[(C_6H_5)_3Sb\begin{matrix}\diagup SNH_4\\ \diagdown SH\end{matrix}\right] \rightarrow (C_6H_5)_3Sb$$

The soluble, yellow, complex compound is very labile and tends to decompose spontaneously if the solution is allowed to stand. In support of his mechanism, Kaufmann has shown that if an equivalent quantity of alcoholic ammonium sulfide is added to an ammoniacal alcoholic solution of triphenylstibinic bromide, the aryl stibinic sulfide precipitates, and that if triphenylstibinic sulfide is treated with alcoholic ammonium sulfide it dissolves. The resulting yellow solution decomposes upon standing, thereby precipitating sulfur and producing a colorless solution from which only triphenylstibine can be isolated. Moreover, if the yellow alcoholic solution of the complex sulfur compound is added to an ammoniacal alcoholic solution of triphenylstibinic chloride, the stibinic sulfide precipitates. Prolonged heating of solutions of the sulfide, treatment with dilute acids—even acetic acid—and heating the solutions in the presence of metals [15] cause decomposition, whereby the free stibine is formed; the last method of decomposition affords an excellent means of obtaining pure triphenylstibine. The analogous tri-m-tolylstibinic sulfide has been prepared similarly, and it is very probable that such sulfides are always formed as intermediates in the conversion of the stibinic chlorides into free stibines by the use of alcoholic ammonia and hydrogen sulfide.

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[13] Morgan, Micklethwait, and Whitby: *J. Chem. Soc.*, 97 (1910), 35.
[14] Kaufmann: *Ber.*, 41 (1908), 2762.

Properties. The triaryl stibinic oxides and hydroxides are solids which have quite definite melting points but which are usually amorphous and insoluble in water but soluble in alcohol. They react with acids to form salts, which are mainly crystalline substances with sharp melting points; there are a few, e.g., the tri-p-tolylstibinic nitrate and sulfate which have not been obtained in the solid state. In the aliphatic series the trimethylstibinic salts are solids, but as the size of the alkyl group increases, the crystallizing power decreases. It is not surprising, therefore, that the salts of the mixed aryl alkyl stibines are solids in the case of phenyl-dimethylstibine but oils in that of phenyl-diethylstibine, and that when the number of alkyl groups is decreased, as in ethyl-diphenylstibine, they are all solids. Crystalline salts are also obtained from the heterocyclic compounds of the type phenyl-cyclotetramethylenestibine. By double decomposition reactions it is possible to convert one salt into another, e.g.:

$$Ar_3SbCl_2 + 2AgNO_3 \xrightarrow{\text{alcohol}} Ar_3Sb(NO_3)_2 + 2AgCl$$

These compounds tend to undergo hydrolysis, and when boiled with water many of them are converted into basic salts. Tri-m-tolylstibinic sulfide when treated with chlorine is converted into the stibinic chloride.

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[15] Kaufmann: Ger. Pat. 240,316.

C. Tertiary Aryl Stibines and Their Derivatives Obtained by Indirect Methods.

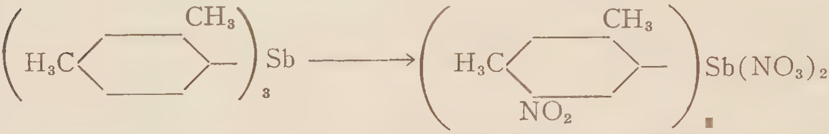
The aromatic stibines which have been discussed up to the present have been only those obtainable by the direct introduction of antimony into the benzene nucleus, but those which are to be taken up for consideration now are prepared from those previously described by reactions involving the aromatic nucleus. It will also be recalled that the reactions of the aromatic stibines which were described above were only those directly related to the antimony atom.

1. Tertiary Nitroaryl Stibines and Their Salts. When triaryl stibines are warmed on the water bath with nitric acid or at about 40° with a mixture of sulfuric and nitric acids, the stibine is not only oxidized to the dinitrate, but nitration of the aromatic nuclei occurs. Instead of the stibine, the hydroxy nitrate may be used as a starting material. Upon dilution of the nitration mixture, the tri-nitroaryl stibinic nitrate was contaminated by some of the corresponding hydroxy nitrate precipitates. The nitrates may be purified as such by repeated crystallization from some anhydrous solvent, or the mixture may be converted into the dihydroxide by solution in aqueous alkali and precipitation with dilute hydrochloric acid. The nitroaryl stibinic nitrate or hydroxide may be reduced to the free stibine by treatment with hydrogen sulfide in alcoholic ammonia; the sulfide probably being an intermediate in this process.

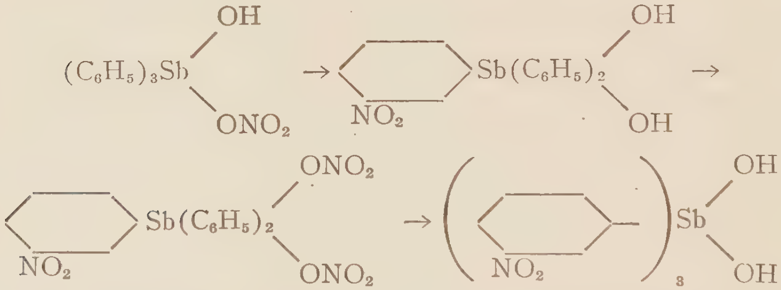
The position taken by the nitro group when it enters the benzene ring is that which is meta to the antimony atom. It has been shown that chlorine in acting on tri-p-anisylstibine severs one of the C-Sb bonds with the introduction of a chlorine atom in the position previously occupied by the antimony. Morgan and Micklethwait[16] utilized this disrupting power of halogens to determine the structure of the trinitro-triphenylstibinic hydroxide obtained by nitration of triphenylstibine, but found it necessary to use bromine as such or in the form of phosphorus pentabromide in chloroform solution at 130°. Under these conditions an excellent yield of

[16] Ref. 2, p. 2291.

m-bromo-nitrobenzene was obtained which indicated that nitration had occurred in the meta position to the antimony atom. Prolonged heating with aqueous bromine at a much higher temperature caused the same decomposition to take place. Iodine chloride in hot acetic acid also eliminates the antimony from the stibine, but the mixture of iodo and chloro derivatives which forms is rather difficult to separate. Similar experiments in which phosphorus pentabromide is heated with the trinitro-tri-m-xylylstibinic nitrate,[17] which may be prepared by nitration of tri-m-xylylstibine, yield 4-bromo-6-nitro-m-xylene. Therefore, in this case also the nitration occurs meta to the antimony atom.



The suggestion[18] has been made that the mechanism of these nitration reactions involves the formation of aryl stibinic nitrates which rearrange to nitro compounds in which the nitro group has entered the meta position.



The migration to the meta position, though unusual, is encountered in the formation of m-nitrobenzoic acid and m-nitraniline from benzoyl nitrate and aniline nitrate respectively.

It was indicated above how the dinitrates, hydroxy-nitrates, and dihydroxides of these nitroaryl stibines may be obtained. The chloride, contaminated by the hydroxy chloride, is formed by boiling the dihydroxide with alcoholic hydrochloric acid. The pure dichloride of trinitro-triphenylstibine is obtained by nitrating triphenylstibinic chloride in sulfuric acid.

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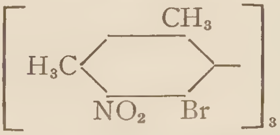
[17] Ref. 3, p. 2315.

[18] Ref. 2, p. 2289.

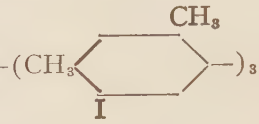
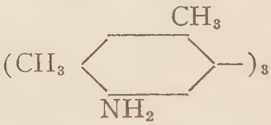
The effect of the negative character of the aromatic nuclei on the properties of the antimony atom was seen in the slight weakening of the affinity of this atom for electro-negative atoms. It is to be expected, therefore, that the magnified negativity of the aryl group resulting from the introduction of nitro groups would be sufficient to bring forth amphoteric properties in the trinitro-triarylstibinic hydroxides. A number of metallic salts of trinitro-triphenylstibinic hydroxide are known; the alkali salts are soluble in water, but those of the alkaline earths and heavy metals are insoluble and are secured from the alkali salts by double decomposition reactions. Also, the nitro groups decrease the strength of the C-Sb union as seen from the formation of small amounts of nitrobenzene when the stibinic hydroxide is boiled in alkaline solution.[19]

In connection with the formation of triaryl stibinic halides by the addition of halogen to the stibine, it was emphasized that this is not universally applicable due to the fact that in some cases halogens not only tend to break the C-Sb bond, but also to enter the aromatic nucleus. An example of this is found in the behavior of tri-5-nitro-tri-m-xylylstibine which forms tri-6-bromo-tri-5-nitro-tri-m-xylylstibinic bromide— 

$SbBr_2$—when treated with bromine in chloroform solution.[20] If the stibinic oxide, instead of the stibine, is brominated, the product is the tri-bromo-stibinic oxide.

2. **Triamino-triaryl stibines.** The nitro groups in the tri-nitroaryl stibines are reduced by zinc and acetic acid or alcoholic hydrochloric acid and tin,[21] but better results are obtained by use of alcohol, ammonium chloride, and zinc. By the latter method tri-m-amino-triphenylstibine[22] and tri-5-amino-tri-m-xylylstibine[23] have been obtained directly from the corresponding nitroaryl stibinic hydroxides or hydroxy nitrates. This reduction is, however, complicated slightly by side reactions one of which involves the splitting of the C-Sb bond.

[19] May: *J. Chem. Soc.*, 97 (1910), 1956.
[20] Ref. 3, p. 2322.
[21] Ref. 19, p. 1958.
[22] Ref. 2, p. 2292.
[23] Ref. 3, p. 2321.

These amino-aryl stibines form readily soluble hydrochlorides, but sparingly soluble diazonium salts; from the latter azo dyes may be obtained. The replacement of the amino group in these stibines by means of the diazo reaction does not proceed smoothly, but tri-5-iodo-tri-m-xylylstibine—  $(CH_3C_6H_2(CH_3)(I)—)_3Sb$ —has been prepared from the corresponding amino compound.[23] Some of the amino aryl stibines, e.g.,  $(CH_3C_6H_2(CH_3)(NH_2)—)_3Sb$ react normally with benzoyl chloride,[23] whereas others are decomposed at the C-Sb linkage by this reagent.

3. The sulfonation of triaryl stibines or their derivatives is much more difficult than the nitration. A trisulfo-triphenylstibinic hydroxide has been prepared by drastic treatment of triphenylstibinic hydroxy sulfate.[24]

D. Dearylation of Stibines, $Ar_3Sb \rightarrow Ar_2Sb — \rightarrow ArSb <$

Except for the small amounts of diphenylstibinic chloride which may be isolated as a by-product in the preparation of triphenylstibine, the methods of preparing aryl stibines yield mainly tertiary compounds. Consequently, it is necessary to adopt indirect processes to secure the primary and secondary aryl stibinous compounds. Michaelis and Reese[25] obtained a mixture of mono and diphenylstibinous chlorides by heating triphenylstibine and antimony trichloride in a sealed tube. Although the reaction has not been extended to other stibines,[26] it gave widely divergent results in the hands of other workers and consequently became the subject of several investigations. Hasenbäumer[27] carried out the experiment in xylene at 240°, and after extracting the unchanged antimony trichloride with dilute aqueous hydrochloric acid and drying the xylene solution, obtained phenylstibinous chloride by fractional distillation at atmospheric pressure but no diphenylstibinous chloride.

[24] Ref. 2, p. 2297.

[25] Michaelis and Reese: *Ber.*, 15 (1882), 2877.

[26] Hasenbäumer: (Ref. 4, p. 2914), applied it to tri-p-tolylstibine.

[27] Hasenbäumer: *Ber.*, 31 (1898), 2910.

Michaelis and Günther,[28] after filtering the xylene solution which had been heated at 240°, did not extract the reaction mixture with dilute hydrochloric acid but subjected it at once to fractional distillation *in vacuo*. After the xylene and unchanged antimony chloride had been distilled off, an oil was obtained which contained some antimony trichloride; the latter was removed by extraction with warm hydrochloric acid. The residual oil solidified to a white crystalline mass of diphenylstibinous chloride which if redistilled underwent partial decomposition with the liberation of antimony trichloride. Morgan and Micklethwait [29] found that, as a result of the reversibility of the reactions, both of the above results are correct; the following equations are given:—

$$2(C_6H_5)_3Sb + SbCl_3 = 3(C_6H_5)_2SbCl$$
$$(C_6H_5)_2SbCl + SbCl_3 \rightleftarrows 2C_6H_5SbCl_2$$

May,[30] like Hasenbäumer, extracted the xylene solution and dried it prior to fractionation; he obtained mainly phenylstibinous chloride and from the higher boiling fractions, some diphenylstibinous chloride and triphenylstibine. Carré,[31] in attempting to fractionate a mixture of mono and diphenylstibinous chlorides, found that both of them tend to revert to triphenylstibine and antimony chloride and that this reversion takes place, although very slowly, at room temperature.

Grüttner and Wiernik [32] investigated the dearylation of triphenylstibine by this method very exhaustively and showed that the contradictions of previous workers were due to the use of different processes in isolating the reaction products. Washing with cold aqueous hydrochloric acid dissolves antimony chloride but neither of the phenylstibinous chlorides, whereas washing with warm acid also dissolves monophenylstibinous chloride; this explains why Michaelis and Günther obtained only diphenylstibinous chloride. Any process of distillation yields an impure product due to the liberation of antimony trichloride. The fraction distilling over the range specified by Hasenbäumer analyzes for phenylstibinous chloride, but the results are meaningless, due to the presence of antimony trichloride as an impurity. After extraction of this distillate

[28] Michaelis and Günther: *Ber.*, 44 (1911), 2316.
[29] Ref. 2, p. 2288.
[30] May: *J. Chem. Soc.*, 101 (1912), 1034.
[31] Carré: *Bull. soc. chim.*, [4] 13 (1913), 102.
[32] Grüttner and Wiernik: *Ber.*, 48 (1915), 1749.

with cold hydrochloric acid, a much lower chlorine value is found, and the residue is a mixture of mono and diphenyl stibinous chlorides. To determine the exact ratio in which the two stibinous chlorides exist in the reaction mixture, the xylene solution was extracted with cold acid, dried, and heated gently in a vacuum to volatilize the solvent. The residual oil was then treated with ethyl magnesium bromide in order to convert the chlorides into tertiary stibines, $C_6H_5(C_2H_5)_2Sb$ and $(C_6H_5)_2C_2H_5Sb$, which were then fractionated *in vacuo*. The results indicated that the mono and diphenyl stibinous chlorides were present in the reaction mixture in the ratio of 1:0.75. When the residue from the evaporation of the xylene was distilled *in vacuo* prior to treatment with the Grignard reagent, the distillate, after removal of the antimony trichloride, contained the mono and diphenyl compounds in the ratio of 1:1.9. After a second distillation and washing with acid, the ratio had become 1:3.8. At no time was any evidence of the formation of triphenylstibine from diphenylstibinous chloride obtained. Therefore, it is evident that phenylstibinous chloride, when heated, gradually forms diphenylstibinous chloride, but the latter substance does not revert to triphenylstibine. By raising the temperature or increasing the time of the original reaction, the yield of the monophenylstibinous chloride is increased at the expense of the diphenyl compound. It is impossible to isolate pure phenylstibinous chloride from the reaction mixture, but material with a low per cent of the diphenyl derivative may be obtained by distilling the crude product rapidly *in vacuo* and extracting with cold hydrochloric acid. Diphenylstibinous chloride may, however, be isolated in the pure state in greatest amounts by washing the crude mixture with acid, heating at about 200° in an atmosphere of carbon dioxide, and again extracting with acid.

In view of the facts that the above method of dearylation produces a mixture of primary and secondary compounds, and that it would be limited to substitution products of triphenylstibine containing groups which would not be altered when exposed to the action of antimony chloride for a long time at a high temperature, Schmidt[33] sought other methods of obtaining the desired reactions. By use of the appropriate reagents it is possible to sever first one and then a second of the C-Sb bonds and thus convert a triaryl stibine into a diaryl stibinous chloride and then into a monoaryl stibinous chloride. In the presence of methyl alcoholic-hydrochloric acid, a triaryl stibine undergoes conversion into a diaryl stibinous chloride; this reaction takes place more readily in some cases than in others, and the temperature and acid concentration must be adjusted to suit the substance in question. Thus, while the solution must be boiled in the case of triphenylstibine, the reaction occurs readily in an ice bath in that of tri-p-acetylamino-triphenylstibine. Care must be exercised not to let the reaction proceed too far, as the diaryl compound may be partly converted into a primary

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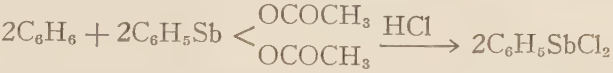
[33] Schmidt: *Ann.*, 429 (1922), 123.

$$(C_6H_5)_3Sb + HCl \xrightarrow{CH_3OH} (C_6H_5)_2SbCl + C_6H_6$$

stibinous chloride. To pass from the diaryl to the monoaryl stibinous chlorides, the secondary stibinous chloride is converted, by treatment with caustic soda, to a stibinous oxide which is dearylated in boiling glacial acetic acid to form a monoaryl stibinous acetate; the latter substance upon treatment with hydrochloric acid is converted into a chloride.

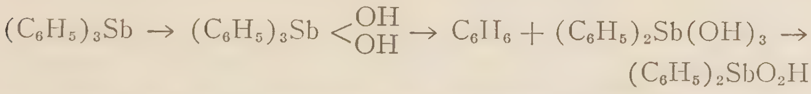
$$2(C_6H_5)_2SbCl + 2NaOH \rightarrow 2NaCl + 2(C_6H_5)_2SbOH \text{ or } [(C_6H_5)_2Sb]_2O + H_2O$$



$$[(C_6H_5)_2Sb]_2O + 4CH_3CO_2H \rightarrow 2C_6H_6 + 2C_6H_5Sb<\begin{matrix}OCOCH_3\\OCOCH_3\end{matrix} \xrightarrow{HCl} 2C_6H_5SbCl_2$$

If the acetic acid is replaced by 100% formic acid, the formation of the primary compound occurs at room temperature.

Another method of dearylation was developed, but in this process the antimony atom is oxidized to the pentavalent condition simultaneously with the splitting of the C-Sb bond. Oxidation of a triaryl stibine with alkaline hydrogen peroxide produces an alkali salt of a diaryl stibinic acid. The experimental conditions under which the reaction will take place vary for different stibines; thus tri-p-acetylamino-triphenylstibine is dearylated in the cold, whereas heat must be applied in the case of triphenylstibine.



$$(C_6H_5)_3Sb \rightarrow (C_6H_5)_3Sb<\begin{matrix}OH\\OH\end{matrix} \rightarrow C_6H_6 + (C_6H_5)_2Sb(OH)_3 \rightarrow (C_6H_5)_2SbO_2H$$

These dearylation processes are important not only because they afford means by which many primary and secondary stibinous chlorides and their various derivatives may be obtained and studied, but as a result of the availability of these two classes of antimonials a new class of tertiary stibines—mixed stibines which could not be obtained directly from antimony trichloride—is opened for study.

$$2Ar_2SbCl + 2Ar'MgBr \rightarrow 2Ar_2Ar'Sb + MgBr_2 + MgCl_2$$
$$ArSbCl_2 + 2Ar'MgBr \rightarrow ArAr'_2Sb + MgBr_2 + MgCl_2$$

The reverse of the above process of dearylation has also been studied by Schmidt,[34] and methods have been developed by which derivatives of primary stibines may be converted into derivatives of secondary stibines and then into tertiary stibines.

$$ArSb< \rightarrow Ar_2Sb— \rightarrow Ar_3Sb$$

Similarly to the reactions described above, these reactions involve the severing of a C-Sb bond, but an antimonial group is eliminated instead of an aromatic residue. In the discussion of the dearylation of triphenylstibine by heating with antimony trichloride, the reversion of phenylstibinous chloride to the diphenylstibinous chloride was described.

When the primary aryl stibinous oxides are heated under carefully controlled conditions, either in the dry state or in certain solvents, antimony oxide is eliminated and either secondary aryl stibinous oxides or tertiary aryl stibines may be obtained.

$$4ArSbO \rightarrow (Ar_2Sb)_2O + Sb_2O_3$$
$$3(Ar_2Sb)_2O \rightarrow 4Ar_3Sb + Sb_2O_3$$

The solvent must be chosen carefully. Thus, while glacial acetic acid is a protecting medium for primary aryl stibinous oxides and converts the secondary oxides into primary oxides, acetic acid containing tartaric acid brings about the reverse change; the influence of the tartaric acid is probably due to its strong tendency to unite with antimony trioxide. Phenylstibinous oxide is readily converted into diphenylstibinous oxide by this method. The following equations are examples of these conversions.

$$4C_6H_5SbO \xrightarrow[\substack{\text{dissolve in acetic} \\ \text{acid containing tartaric acid}}]{\text{4 hrs. at } 100°\text{; or}} [(C_6H_5)_2Sb]_2O + Sb_2O_3$$

$$4(m\text{-}HCl \cdot H_2NC_6H_4)SbCl_2 + 3H_2O \xrightarrow[\substack{\text{dilute water} \\ \text{solution}}]{\text{reflux 1 hr. in}}$$
$$2(m\text{-}HCl \cdot NH_2C_6H_4)_2SbCl + Sb_2O_3 + 6HCl$$

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[34] Schmidt: *Ann.*, 421 (1920), 214, 233.

$$3C_6H_5SbO \xrightarrow{\text{4 hrs. at 180–200°}} (C_6H_5)_3Sb + Sb_2O_3$$

$$3(m\text{-}NH_2C_6H_4)SbO \xrightarrow{\text{1 hr. at 120–125°}} (m\text{-}NH_2C_6H_4)_3Sb + Sb_2O_3$$

$$3(p\text{-}CH_3CONHC_6H_4)SbO \xrightarrow[\text{in } CH_3OH]{\text{reflux 3 hrs.}} (p\text{-}CH_3CONHC_6H_4)_3Sb + Sb_2O_3$$

It is, of course, understood that in both dearylation and "de-antimonalization," as the latter reactions may be termed, those reactions which require the application of heat to either the dry substance or its solutions, should be carried out in an inert atmosphere to avoid the formation of pentavalent antimonials.

Owing to the fact that primary aryl stibinous oxides are obtainable from aryl stibinic acids, a great variety of which have become available through the application of the diazo-reaction to the production of antimonials, the conversion of these primary oxides into secondary oxides and tertiary stibines affords a method of preparing many members of these latter two classes of antimonials which could not be obtained by other processes. Two of the tertiary stibines, tri-m-amino-triphenylstibine and tri-p-acetylamino-triphenylstibine, which have been prepared by these methods have been found to exist in two and three modifications respectively which differ in melting point, solubility, and water content. In both instances the modifications are interconvertible.[35]

E. Primary and Secondary Aryl Stibinous Halides and Their Derivatives.

Although the primary and secondary aryl stibines are as yet unknown, many of their derivatives have been studied. These substances cannot be obtained by the direct introduction of antimony into an organic molecule but must be prepared by the indirect methods which were discussed above and which will be summarized briefly by equations.

$$Ar_3Sb + SbCl_3 \xrightarrow{\text{heat}} ArSbCl_2 + Ar_2SbCl$$

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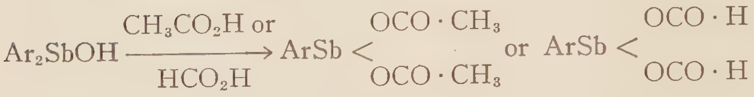
[35] Ref. 6, p. 124; Ref. 34, p. 243.

$$Ar_3Sb \xrightarrow{CH_3OH \cdot HCl} Ar_2SbCl$$

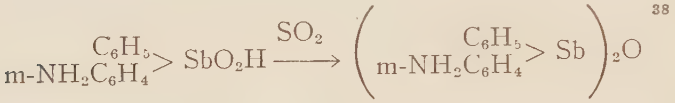


$$Ar_2SbOH \xrightarrow[HCO_2H]{CH_3CO_2H \text{ or}} ArSb < \begin{matrix} OCO \cdot CH_3 \\ OCO \cdot CH_3 \end{matrix} \text{ or } ArSb < \begin{matrix} OCO \cdot H \\ OCO \cdot H \end{matrix}$$

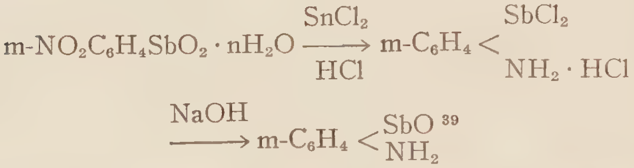
$$ArSbO \xrightarrow{\text{heat}} Ar_2SbOH$$

The primary and secondary stibinous oxides may also be obtained from aryl stibinic acids by reduction, e.g.:

$$C_6H_5SbO_2 \cdot nH_2O \text{ [36]} \xrightarrow{SO_2 + HI} C_6H_5SbO \text{ [37]}$$



$$\begin{matrix} C_6H_5 \\ m\text{-}NH_2C_6H_4 \end{matrix} > SbO_2H \xrightarrow{SO_2} \left(\begin{matrix} C_6H_5 \\ m\text{-}NH_2C_6H_4 \end{matrix} > Sb \right)_2 O \text{ [38]}$$



$$m\text{-}NO_2C_6H_4SbO_2 \cdot nH_2O \xrightarrow[HCl]{SnCl_2} m\text{-}C_6H_4 < \begin{matrix} SbCl_2 \\ NH_2 \cdot HCl \end{matrix}$$

$$\xrightarrow{NaOH} m\text{-}C_6H_4 < \begin{matrix} SbO \\ NH_2 \end{matrix} \text{ [39]}$$

In carrying out the last reaction, the stibinous chloride may be isolated.[40]

The salts of the aryl stibinous oxides may be prepared either by treating the oxides with acids, or by converting one salt into another by double decomposition reactions.

$$ArSbO \xrightarrow{H_2S} ArSbS$$

$$ArSbCl_2 \xrightarrow{NaI} ArSbI_2$$

Properties. The primary and secondary aryl stibinous oxides and salts are solids which, with the exception of the amorphous primary oxides, are crystalline. Although the oxides have slightly indefinite melting points, the salts melt quite sharply. Unless the aromatic nucleus contains some salt forming group, the oxides and salts of this series are insoluble in water. The stability of these substances varies greatly; as shown above, members of the primary series are converted under certain conditions into members of the secondary or tertiary series by the elimination of antimony, while under other conditions the secondary compounds change, with the loss of an aryl group, into primary compounds. Consequently, in all reactions involving substances of these types the ease with which the C-Sb linkage is broken must be kept in mind.

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[36] The representation of primary aryl stibinic acids by the formula $ArSbO_2.nH_2O$ instead of $ArSbO_3H_2$ will be discussed later.

[37] Ref. 34, p. 217.

[38] Ger. Pat. 269,206.

[39] Ref. 30, p. 1035.

[40] Ref. 34, p. 223.

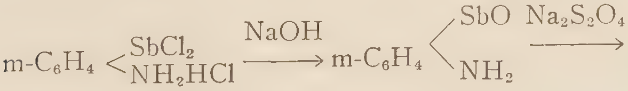
The primary and secondary stibinous oxides do not possess the amphoteric nature of antimony trioxide; they are distinctly more basic than this substance and do not dissolve readily in alkalies. However, they react readily with halogen acids to form primary and secondary aryl stibinous halides, $ArSbX_2$ and Ar_2SbX, in which the halogen is held much more firmly than in antimony trichloride; this is evident from the fact that aryl stibinous halides are hydrolyzed very slightly as compared with antimony trihalides. The oxides also dissolve in acetic and formic acids forming the acetates and formates. Further evidence of salt formation is found in the formation of insoluble sulfates and oxalates when ether solutions of the oxides are shaken with aqueous sulfuric or oxalic acids, and the formation of a sulfide when the oxide is treated in alcoholic ammonia with hydrogen sulfide. In the presence of alkalies, the oxides are oxidized by hydrogen peroxide to mono or diaryl stibinic acids.

$$\text{m-}NH_2C_6H_4SbO \xrightarrow{H_2O_2} \text{m-}NH_2SbO_2 \cdot nH_2O$$ [41]

$$(\text{p-}CH_3CONHC_6H_4)_2SbOH \xrightarrow{H_2O_2} (\text{p-}CH_3CONHC_6H_4)_2SbO_2H$$ [42]

The primary oxides may be reduced by reagents such as sodium hypophosphite and sodium hydrosulfite to aryl stibino compounds.

$$2C_6H_5SbO \xrightarrow{NaH_2PO_2} C_6H_5Sb = SbC_6H_5$$ [43]



$$\text{m-}C_6H_4 < \begin{matrix} SbCl_2 \\ NH_2HCl \end{matrix} \xrightarrow{NaOH} \text{m-}C_6H_4 \begin{matrix} \diagup SbO \\ \diagdown NH_2 \end{matrix} \xrightarrow{Na_2S_2O_4}$$

$$\text{m-}NH_2C_6H_4Sb = SbC_6H_4NH_2\text{-m}$$ [44]

[41a] Ref. 39.

[b] Ref. 34, p. 226.

[42] Ref. 6, p. 138.

[43] Ref. 34, p. 221.

[44] Ger. Pat. 268,451.

The secondary oxides also yield reduction products but these have not been investigated to any great extent. Diphenylstibinous oxide, when treated with hypophosphorous acid, is reduced to a yellow substance which may be tetraphenyl-distibine—$(C_6H_5)_2Sb\text{-}Sb(C_6H_5)_2$.[45]

Of the salts of the primary and secondary aryl stibinous oxides, the chlorides have been used and studied more than any of the others, in some cases the acetates, iodides and sulfides have also been examined. The stibinous chlorides are only slightly hydrolyzed by water, but are readily decomposed by alkaline reagents, e.g., carbonates and hydroxides, into the oxides. When treated with sodium iodide, the chlorides are converted into aryl stibinous iodides[46] which are yellow crystalline substances; the acetates are converted into the chlorides by hydrochloric acid. The chlorides in alcoholic ammonia react with hydrogen sulfide forming aryl stibinous sulfides; of course, the chloride is first converted into the hydroxide by the ammonia.

A reaction of the chlorides, which was used extensively in the early studies of aromatic antimonials, involves the addition of chlorine to form crystalline aryl stibinic chlorides, $ArSbCl_4$ and Ar_2SbCl_3, which, upon hydrolysis, yield primary and secondary stibinic acids. Phenylstibinic chloride, like antimony pentachloride, is dissociated by heat with the elimination of two atoms of chlorine, and the resulting phenylstibinous chloride then partially decomposes, forming some diphenylstibinous chloride and antimony trichloride. If the experiment is performed in a closed tube, the primary and secondary phenylstibinous chlorides reunite with the chlorine upon cooling to form a mixture of stibinic chlorides. p-Anisylstibinic chloride, however, decomposes in a similar manner even at room temperature. The ease with which the C-Sb bond is broken in the tetrachlorides explains the tendency of many of the stibinic acids to decompose to some extent in the presence of hydrochloric acid.

The condensation of primary aryl stibinous chlorides and primary aryl arsines with the elimination of hydrogen chloride has been used in the preparation of arseno-stibino compounds;[47] in this reaction the chloride may be replaced by the oxide.

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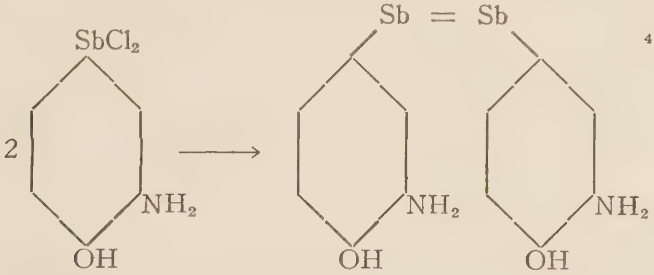
[45] Ref. 34, p. 235.
[46] Ref. 34, p. 218, 225.
[47] Ehrlich and Karrer: *Ber.,* 46 (1913), 3564.

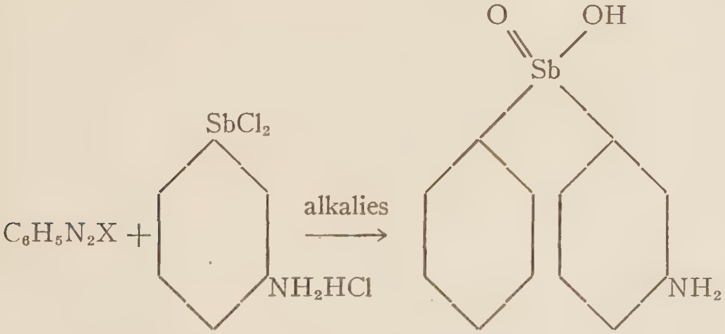
$$ArAsH_2 + Cl_2SbAr \rightarrow ArAs = SbAr + 2HCl$$

When reduced with hypophosphorous acid in the presence of sodium hypophosphite, the stibinous chlorides are converted into stibino compounds; the sodium hypophosphite is added in order to avoid the formation of free hydrochloric acid.



[48]

The formation of mixed aryl and aryl alkyl stibines from the stibinous chlorides by the action of Grignard reagents has already been mentioned. When added to an alkaline solution of a diazonium salt, the primary aryl stibinous chlorides react to form secondary aryl stibinic acids; this will be discussed in connection with the production of stibinic acids.



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[48] Ref. 6, p. 151.

Chapter 4.

Aromatic Stibinic Acids and Aromatic Stibino Compounds.

A. Primary Aromatic Stibinic Acids.

Research in this field of organic antimonials was limited to the study of a very few compounds prior to the discovery that the versatile diazo reaction can be applied to the production of stibinic acids. Attempts to "stibinate" aromatic compounds by treatment with antimonic acid in the manner that arsenation may be carried out by use of arsenic acid all met with failure, and the statement that primary aryl stibinous chlorides may be obtained by the action of antimony trichloride on aniline[1] in a manner analogous to that in which p-dimethylaminophenylarsenious chloride is secured from dimethylaniline and arsenious chloride was found to be erroneous.[2] Consequently, the only remaining source of these substances was the triaryl stibines; it is obvious that starting from such a point necessitated the application of a "dearylation" process, and prior to Schmidt's very recent studies, the only available one was that in which the tertiary stibine is heated with antimony trichloride. Inasmuch as dearylation by this method had been applied only to triphenyl and tri-p-tolyl stibine, the investigations of the aryl stibinic acids were confined solely to phenyl and p-tolyl stibinic acids and a few of the substitution products, such as nitrophenylstibinic acid, which could be obtained from them.

Preparation. 1. Although, in the light of the later studies on the dearylation of triphenylstibine, the phenyl and p-tolyl stibinous chlorides which Hasenbäumer obtained must have been at least slightly impure, he showed that when aryl stibinic chlorides, which may be prepared by the addition of chlorine to the stibinous chlorides, are hydrolyzed by dilute alkalies, aryl stibinic acids are obtained.[3]

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[1] Breinl and Nierenstein: *Annals of Trop. Medicine and Parasit.* (1908-9) II, 379.

[2] May: "The Chemistry of Synthetic Drugs," Longmans (1918), p. 215.

$$ArSbCl_2 \rightarrow ArSbCl_4 \rightarrow ArSbO_2 \cdot nH_2O$$

Due to the presence of at least some diaryl stibinous chlorides in his starting materials it is very probable that Hasenbäumer's stibinic acids were not pure, because the diaryl stibinous chlorides are converted in a similar manner into diaryl stibinic acids.

$$Ar_2SbCl \rightarrow Ar_2SbCl_3 \rightarrow Ar_2SbO_2H$$

Nevertheless, if pure monoaryl stibinous chlorides are available this process may be employed for the preparation of aryl stibinic acids.

2. Another method involving the oxidation of trivalent antimonials depends upon the oxidation of monoaryl stibinous oxides in alkaline solution with hydrogen peroxide.

However, since the only method by which the pure monoaryl stibinous chlorides or oxides may be obtained conveniently and in any degree of variety is by reduction of the stibinic acids, and since the primary stibinous chlorides and oxides tend to lose part of their antimony very readily, thereby forming secondary aryl stibinous chlorides and oxides, the two methods outlined above are of only passing interest.

3. The only useful method of preparing aryl stibinic acids depends upon the replacement of the diazo group by an antimonial group when a diazonium salt is treated with antimony trioxide in the presence of alkali.[4] In those instances where the aromatic amine contains a nitro group, it is advisable to operate in neutral or even slightly acid solution.

$$ArN_2OH + NaH_2SbO_3 \rightarrow ArSbO_3HNa + N_2 + H_2O$$

In spite of the fact that many patents were taken out describing the preparation of a number of different stibinic acids by this process and the conversion of these acids into other antimonials, no discussion of this reaction or the properties of these acids appeared in the scientific journals till very recently.[5]

The mechanism of this reaction may be represented in several ways. The antimony oxide, in order to enter into the reaction, must be in its hydrated form, i.e., as antimonious acid, which, as Schmidt suggests, may be capable of existing in the tautomeric forms represented by I and II in which tri and pentavalent antimony are present respectively.

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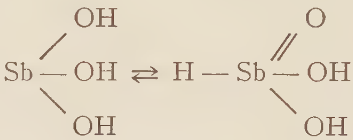
[3] Hasenbäumer: *Ber.,* 31 (1898), 2910 wrote the formulæ as $ArSbO_3H_2$ probably because similar formulæ express the composition of the analogous arsenicals. As will be shown later, this formula is not correct.

[4] Ger. Pat. 254,421 (1912).

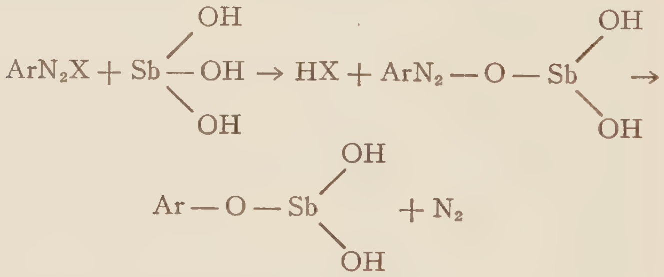
[5] Schmidt: *Ann.,* 421 (1920), 174.



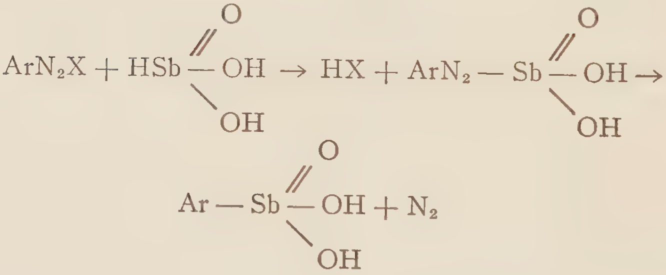
I II

If the reaction involves an elimination process between the diazo compound and the antimonious oxide to form a diazo-antimonial which subsequently loses its nitrogen, the steps may be represented in the following ways.[6]

(a)



(b)



A compound of the type $Ar-O-Sb<^{OH}_{OH}$ such as would be obtained by mechanism (a) would, since it is an aryl ester of antimonious acid, be extremely unstable and undergo instantaneous hydrolysis to a phenol and antimonious acid.[7] Consequently, if the reaction involves elimination of HX prior to formation of the diazo antimonial it is apparently necessary to adopt the view that antimonious acid enters the reaction in form II.

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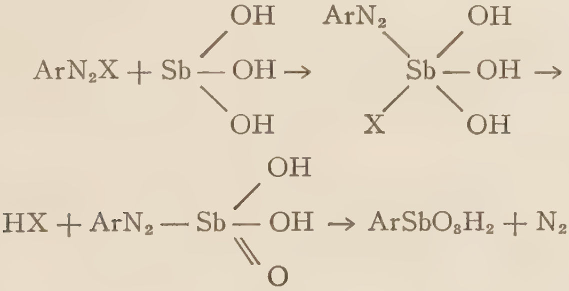
[6] Inasmuch as the reaction is carried out either in slightly acid, neutral, or alkaline solution depending upon the nature of the aryl amine being used, the reactions will be written as taking place between a diazo compound and antimonious oxide without inserting the caustic or acid which is used.

There is, however, an alternative way in which the same end may be attained. Throughout the chemistry of the antimonials the tendency of the trivalent antimonials to enter into addition reactions and thereby become derivatives of pentavalent antimony has been noted. It is possible that the diazo compound adds to the antimonious acid before elimination of HX takes place; if this is true, antimonious acid can react only in form I.

(c)



$$ArN_2X + Sb(OH)_3 \rightarrow ArN_2Sb(X)(OH)_3 \rightarrow$$

$$HX + ArN_2—Sb(=O)(OH)_2 \rightarrow ArSbO_3H_2 + N_2$$

III

In both (b) and (c) a diazo-stibinic acid is an intermediate, and it is from this substance that the nitrogen is evolved. Although in some cases the addition of copper facilitates this part of the reaction, the presence of copper is not absolutely necessary; usually the nitrogen is evolved very readily in the cold without the aid of any catalyst. The ease with which the diazo-stibinic acid decomposes indicates that the Sb-N bond must be very weak.

During the formation of aryl stibinic acids by the diazo method side reactions always take place whereby dyestuffs and reduction products are produced; the latter reaction can be controlled to a considerable extent. The reduction process involves the elimination of nitrogen and the formation of antimonic acid and an aromatic compound containing hydrogen in the position originally occupied by the amino group.

$$ArN_2OH + Sb(OH)_3 \rightarrow ArH + H_3SbO_4 + N_2$$

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[7] Mackey: *J. Chem. Soc.*, 95 (1909), 604 prepared a number of alkyl and aryl esters of antimonious acid; although they were found to be stable under anhydrous conditions, water hydrolyzed them immediately.

According to the theory of diazo reactions the replacement of the diazo group takes place through the syn-diazo compound while the reduction processes involve the anti compound. Consequently, it is desirable to so adjust the experimental conditions that the anti-diazo compound will be formed to the smallest possible extent. Since the conversion of the syn to the anti configuration is markedly influenced by the hydrogen ion concentration of the reaction medium and by the nature of substituent groups attached to the benzene nucleus, the alkalinity of the solution must be carefully controlled and adjusted for each compound if reduction processes are to be kept at a minimum. In general, in applying this reaction to the production of antimonials, the reaction mixture may be kept more alkaline than is permissible in corresponding reactions in the arsenical series. The arsonic acid group unlike the nitro group, when present in a diazo compound does not cause undesirable results, reduction processes, when the reaction with antimonious oxide is carried out in alkaline solution.

As antimony trioxide is the anhydride of a very feeble acid, it does not dissolve to any great extent in solutions which are only slightly alkaline, but if freshly precipitated material, i.e., hydrated antimony trioxide, is used, it is not essential that it be dissolved in order to obtain successful results with this reaction. The antimony may be added to the reaction mixture in the form of a soluble compound, tartar emetic, which in both alkaline and acid solutions yields precipitates of hydrated antimony oxide.

May,[8] during his study of the behavior of diazonium chlorides to antimony trichloride, came very close to discovering that aryl stibinic acids may be prepared by means of the diazo-reaction. Diazonium chlorides and antimony trichloride in acid solution form very stable, insoluble, crystalline double salts, which may be kept in the dry state without any danger of explosion unless heat is applied. The tendency for this compound to form is so great that a diazonium chloride will remove the metallic chloride completely from a hydrochloric acid solution of it. Generally, these addition compounds contain the constituent molecules in the ratio of 1 : 1. When heated in the presence of water they decompose; benzene diazonium chloride-antimony trichloride when heated in water loses its nitrogen and is converted into phenol, diphenyl and antimony pentachloride. The addition of sodium hydroxide to a suspension of May's double salt

[8] May: *J. Chem. Soc.,* **101** (1912), 1037.

in cold water causes the evolution of nitrogen and the formation of phenylstibinic acid.[9] This modification of the diazo-reaction gives excellent results in the preparation of stibinic acids, and evolution of nitrogen is much more gradual than when the other method is employed.[10]

Instead of adding a solution of a diazonium salt to alkaline antimony trioxide or actually isolating the molecular compound, a hydrochloric acid solution of the amine and antimony trichloride may be diazotized and then made alkaline.[9b]

The diazo-reaction has been used to prepare aromatic stibinic acids containing a great variety of substituents, e.g., halogens, nitro, hydroxyl, alkoxyl, alkyl, acyl-amino groups, in the benzene ring, and from these, numerous other stibinic acids can be prepared by the usual processes employed in the formation of aromatic compounds. In those cases in which diazotization of the aromatic amine does not proceed smoothly due to the influence of certain of the substituent groups, it is necessary to adopt an indirect method of preparation. An example of this is the case of m-nitrophenylstibinic acid which cannot be obtained readily from m-nitroaniline; excellent results are, however, secured by the nitration of phenylstibinic acid.[11]

Properties. The primary aryl stibinic acids are for the most part amorphous, non-melting solids, which are insoluble in water; some of these acids may be obtained in a crystalline condition from organic solvents. They are soluble in caustic alkalies, alkali carbonates, and ammonia but give insoluble salts with the heavy metals. These substances, like antimonic acid, are amphoteric and dissolve in concentrated hydrochloric acid, forming aryl stibinic chlorides.

A discussion of Schmidt's conception of the structure of the aryl stibinic acids, may well be prefaced by a few remarks on the

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[9a] Ger. Pat. 261,825.

[b] Ref. 5, p. 177.

[10a] Antimony halides possess the property of forming crystalline molecular compounds with organic substances to a remarkable degree. Thus, antimony trichloride unites with aromatic hydrocarbons, amines, halides, and nitro compounds to produce molecular compounds; and antimony pentachloride reacts similarly with alcohols, aldehydes, ketones, esters, acid chlorides, hydrochlorides of heterocyclic nitrogen bases, quinones, aryl amine hydrochlorides, and aromatic hydrocarbons.

[b] Pfeiffer: *Zeit. anorg. Chem.*, 133 (1924), 101. Antimony pentachloride and ethyl oxalate form an addition compound $(CO_2C_2H_5)_2.2SbCl_5$ which when heated loses ethyl chloride and yields a salt of oxalic acid $[CO_2(SbCl_4)]_2$.

[11] Morgan and Micklethwait: *J. Chem. Soc.*, 99 (1911), 2286, showed that the stibinic acid group directs entering groups to the meta position.

inorganic antimonic acids. When pyroantimonic acid is neutralized to phenolphthalein with sodium hydroxide, it yields an aqueous solution which upon standing, or more rapidly upon boiling, becomes acid due to the formation—by hydration of the sodium pyroantimonate—of acid sodium orthoantimonate. By alternate neutralization and boiling, a solution of sodium orthoantimonate is secured which does not undergo any further change in alkalinity with respect to phenolphthalein. Of course, when the ortho acid, which may be obtained by boiling the pyro acid in water solution, is neutralized to phenolphthalein with sodium hydroxide, it immediately yields a solution which does not become acid again.[12] The number of hydrates of antimonic oxide which are known is quite large, and the degree of hydration varies from $Sb_2O_5 \cdot 6H_2O$ to Sb_2O_5 depending upon the method of preparation and the conditions of drying.[13] The tetra hydrate, $Sb_2O_5 \cdot 4H_2O$, and the trihydrate,[14] $Sb_2O_5 \cdot 3H_2O$, into which it changes, would be expected to be ortho antimonic acids, but they readily lose two and one molecules of water respectively when dried over sulfuric acid or at 100°, whereas ortho antimonic acid changes to pyroantimonic acid only at a higher temperature. Also, both hydrates when neutralized to phenolphthalein with sodium hydroxide yield aqueous solutions which, on standing, become acid and require the further addition of alkali; after alternate standing and neutralization with alkali, a solution is finally obtained which does not undergo any further change; they behave like pyro acids. Therefore, these hydrates, although possessing a total water content sufficient to enable them to be represented as ortho acids are in reality pyro acids containing varying amounts of loosely bound water which is not water of constitution, and they should be written as $(H_4Sb_2O_7)2H_2O$ and $(H_4Sb_2O_7)H_2O$ respectively.

Phenylstibinic acid may be obtained in different degrees of hydration depending upon the method of preparation[15] and the conditions of drying and may be represented by the empirical formulæ $3C_6H_5SbO_2 \cdot 3H_2O$ and $3C_6H_5SbO_2 \cdot 4H_2O$[16] which could also be written $C_6H_5SbO_3H_2$ and $C_6H_5SbO_3H_2 \cdot H_2O$ without altering the proportions of the constituents. The latter is the method of formulation originally adopted by Hasenbäumer[17] and other investigators in this field. These products, however, readily lose 2 and 3 molecules of water respectively when dried *in vacuo* over sulfuric acid,[18] but they must be heated to temperatures well above 100° to remove the remaining molecule of water. Consequently, since only a portion of the water appears to be water of constitution, the above formulæ for phenylstibinic acid should be written $[3(C_6H_5SbO_2)H_2O]2H_2O$ and $[3(C_6H_5SbO_2)H_2O]3H_2O$, and this substance, like the tri and tetra hydrates of antimony oxide mentioned above, is a derivative not of ortho antimonic acid, but of a partially dehydrated ortho acid and contains additional amounts of loosely bound water.

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[12] Delacroix: *J. de Pharm.*, [6] 6 (1897), 337.

[13] Senderens: *Bull. soc. chim.*, [3] 21 (1899), 53.

[14] Delacroix: *Ibid.*, [3] 21 (1899), 1049; [3] 25 (1901), 288.

[15] In general, arylstibinic acids prepared by hydrolysis of arylstibinic chlorides ($ArSbCl_4$) retain more water than those formed by treating solutions of alkali arylstibinates with mineral acids.

[16] Ref. 5, p. 192.

This method of formulation is further supported by the behavior of phenylstibinic acid toward alkali. If this acid were a derivative of ortho antimonic acid, it would react immediately with one molecule of sodium hydroxide to yield a solution which would not only be neutral to phenolphthalein but unaffected by standing or heating. This is not the case, however. Phenylstibinic acid dissolves completely in ⅓ of a molecular equivalent of sodium hydroxide, and the resulting solution, although initially neutral to phenolphthalein, soon gives an acid reaction and requires the addition of more alkali. If the solution is neutralized after each period of standing, a condition of permanent neutrality is finally reached after a total of 1 molecular equivalent of alkali has been added. This indicates definitely that instead of being a derivative of ortho antimonic acid, $(HO)_3SbO$, formed by replacement of one hydroxyl group by a phenyl group, phenylstibinic acid is a complex molecule resulting from the association of three molecules of the phenyl derivative of ortho antimonic acid, $C_6H_5SbO_3H_2$. The process of association is accompanied by the removal of two molecules of water from direct union with the antimony atoms to a sphere in which they are held to the molecule by comparatively weak forces. The complex molecule is not a polymer of $C_6H_5SbO_3H_2$ in the sense that three molecules have become associated as such, because part of the water has been displaced to a field in which it is held by weak forces as shown by the ease with which it may be removed. The phenomenon observed during the treatment with alkali is one of hydration of the

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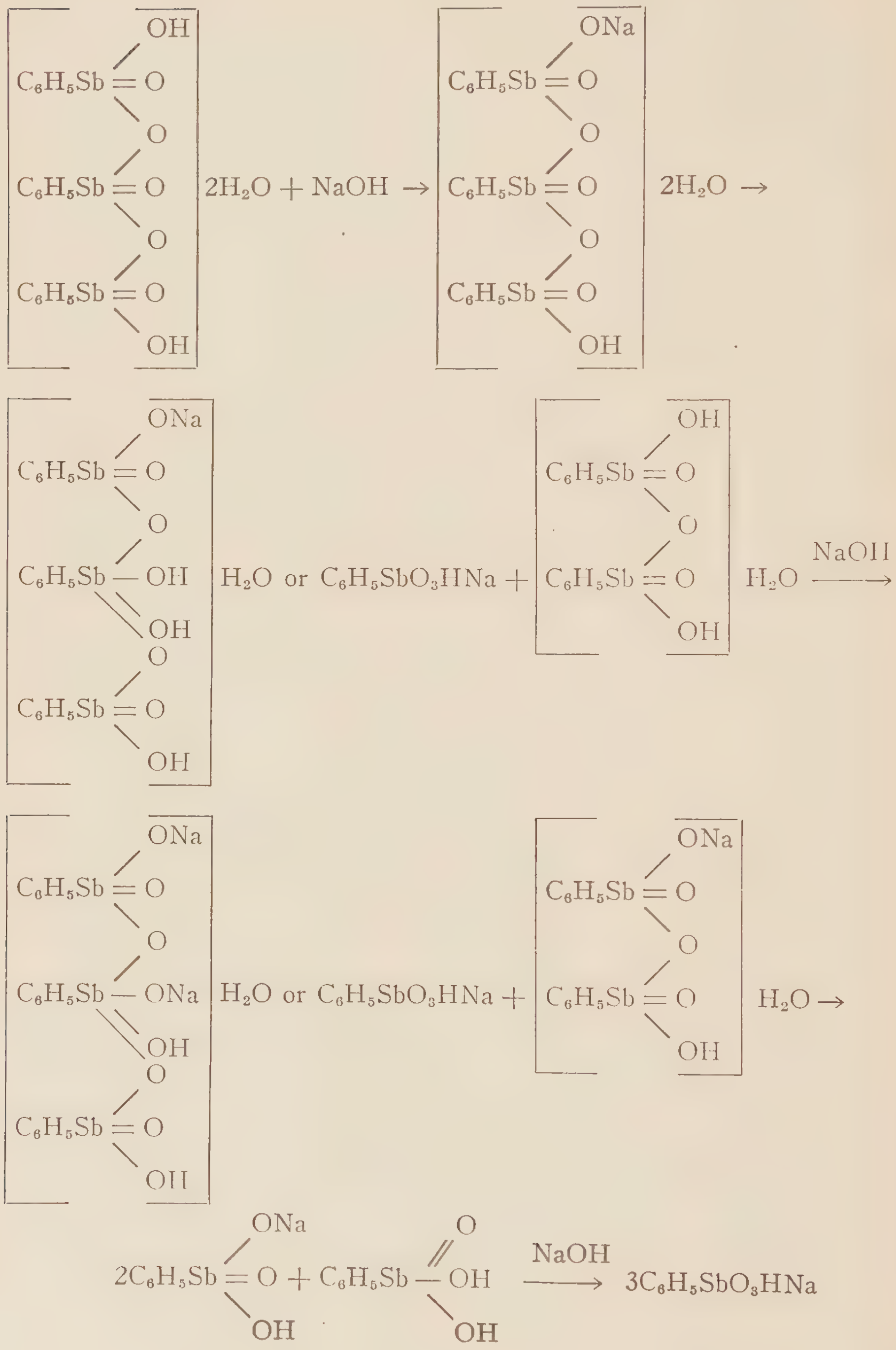
[17] Hasenbäumer: *Ber.*, 31 (1898), 2910.

[18] Upon exposure to the air the after drying *in vacuo*, water is absorbed, but the water content never becomes quite as high as in the original, air-dried material.



antimony atoms whereby the complex is dissociated into the phenyl derivative of ortho antimonic acid. That phenylstibinic acid can exist as a true derivative of an ortho acid only while in the form of its alkali salt is evident from the fact that upon acidification the organic antimonial gradually reverts to its original complex form. The hydration reaction takes place with approximately the same degree of ease with either sodium or potassium hydroxide but less readily in the presence of lithium hydroxide.[19]

Existence in a complex state is not limited to phenylstibinic acid but extends to all the primary aryl stibinic acids; the presence of substituents in the benzene nucleus, however, has a distinct bearing on the nature of the complex and on its dissociation in the presence of alkali. In the negatively substituted acids, the complex molecule is also formed by the association of three of the simple molecules, but in this case only one of the water molecules has been removed to a position in which it is feebly bound and the remaining two can not be removed by drying *in vacuo,* e.g.

$$3ClC_6H_4SbO_3H_2 \rightarrow [3(ClC_6H_4SbO_2)\cdot 2H_2O]H_2O$$

When these negatively substituted products are isolated from water solution, they contain, in addition to the one molecule of loosely held water resulting from the association process, water of crystallization which is also easily removable in a vacuum desiccator. Thus, p-chlorophenylstibinic acid is represented by the formula, $[3(ClC_6H_4SbO_2)2H_2O]3H_2O$. Inasmuch as negative substituents decrease the extent to which water is removed from the central antimony atoms during the formation of the complex, and since the dissociating action of alkali involves the hydration of these atoms, the chlorophenylstibinic acids should undergo conversion into derivatives of ortho antimonic acid more rapidly than the unsubstituted acid does; this has been found to be true experimentally. Conversely, although the positively substituted acids still retain one molecule of water firmly attached to the antimony atoms in the complex molecule, e.g., m-amino-phenylstibinic acid is $[3(NH_2C_6H_4SbO_2)H_2O]4H_2O$, the rate of hydration during the dissociation of the complex by means of alkali is less than in the case of phenylstibinic acid.

The complex nature of these acids and the gradual hydration induced by alkalies are the sources of the difficulties encountered in isolating salts of the aryl stibinic acids which will redissolve in water forming neutral solutions. Solutions of phenylstibinic acid in caustic soda differ markedly depending upon whether hydration has been permitted to take place. Thus, the initial solution of phenylstibinic acid in just sufficient sodium hydroxide to dissolve it yields a precipitate of a sodium salt when treated with concentrated caustic soda or salt solution, whereas after complete dissociation of the complex, precipitation does not occur.

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[19] Schmidt: *Ber.,* 55 (1922), 697.

This conception of the structure of these acids is supported by analyses of the neutral sodium salts of several of the stibinic acids.[20]

TABLE III

Composition of Neutral Sodium Aryl Stibinates

Neutral Sodium Salt of	*Atomic Ratio Na:Sb*
Phenylstibinic acid	1:2.06
m-Acetylaminophenylstibinic acid	1:2.9
p-Acetylaminophenylstibinic acid	1:2.8
p-Bromophenylstibinic acid	1:1.35
p-Ethoxyphenylstibinic acid	1:1.27

In every instance there is less than one atom of sodium per atom of antimony, and the salts of the two acetyl acids contain practically three atoms of antimony per atom of sodium. Therefore, these salts, which dissolve in water forming neutral solutions, appear to be mono sodium salts of the complex, associated acids, in which the ratio of Na : Sb should be 1 : 3, mixed with varying quantities of the sodium salts of the hydrated acids, $ArSbO_3H_2$. If the stibinic acids were unassociated derivatives of ortho antimonic acid, the composition of the neutral salts would be such that the Na : Sb ratio would be 1 : 1, i.e. $ArSbO_3HNa$.

Macallum[21] does not accept Schmidt's conception of the structure of the stibinic acids and prefers to represent them as monomolecular derivatives of ortho antimonic acid, $ArSbO_3H_2$. Molecular weight determinations by the cryoscopic method using p-nitro and p-aminophenylstibinic acids dissolved in phenol and formic acid respectively indicate that, under the experimental conditions employed, these two substances are monomolecular. The complete data from which the molecular weights were calculated are not reported, and inasmuch as these conclusions do not agree with those previously set forth, the matter should be investigated much more thoroughly and all the experimental data should be recorded.

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[20] Fargher and Gray: *J. Pharm. and Exper. Therap.*, 18 (1921), 353.
[21] Macallum: *J. Soc. Chem. Ind.*, 42 (1923), 468T.

Jander[22] studied the various hydrates of antimony pentoxide and concluded that the tri and tetra hydrates, to which the arylstibinic acids have been compared, possess the properties of colloids. Therefore, the appearance of colloidal characteristics in the aryl stibinic acid series is not unexpected. When an alkaline solution, i.e., a dissociated solution, of one of these acids is titrated back with a mineral acid, it remains clear at first and then gradually becomes turbid; when a quantity of acid equivalent to the total amount of alkali originally present has been added, the turbidity is very intense. The presence of substituents in the aromatic nucleus affects the colloidal properties of the stibinic acids very greatly. If strongly negative substituents are present, or if acetic acid is used for the back titration, the solution merely becomes opalescent. The turbid solutions of the stibinic acids possess the characteristics of hydrosols.[23] It is only by the addition of an excess of acid—the extent of this excess varies in different cases—that the colloidal stibinic acids are precipitated from the turbid solutions. Further evidence of the colloidal nature of these substances is found in the facts that during the filtration and washing of the precipitates the final washings contain some of the stibinic acid in colloidal suspension, that the washed and dried material frequently regelatinizes in water, that small amounts of alkali exert a peptizing action on many of the stibinic acids, and that solvents for the colloidal cellulose esters frequently dissolve aryl stibinic acids.

The aryl stibinic acids are readily converted by the action of hydrochloric acid into aryl stibinic chlorides which, with few exceptions, dissolve in concentrated hydrochloric acid forming arylchlorostibinic acids, $ArSbCl_5H$, analogous to chloroantimonic acid, $HSbCl_6$.[24] Many of these solutions deposit crystalline products which, after drying, are found to be the aryl stibinic chlorides, $ArSbCl_4 \cdot nH_2O$; there is evidence that during the process of drying a molecule of hydrochloric acid is lost, thereby indicating that the original crystalline material was an arylchlorostibinic acid. Water hydrolyzes arylstibinic chlorides readily to stibinic acids. Although the arylchlorostibinic acids cannot be isolated as such, characteristic salts may be obtained with ease by treating a hydrochloric acid solution of the chloride with ammonium chloride or a substituted ammonium chloride. The formation of such salts of arylchlorostibinic acids is of great assistance in the isolation and purification of aryl stibinic acids, because they may be hydrolyzed readily to the stibinic acids.

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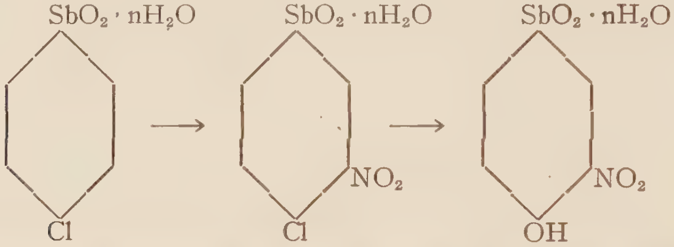
[22] Jander: *Kolloid-Zeitschr.*, 23 (1918), 122.
[23] Ref. 5, p. 182.
[24] Weinland and Schmid: *Zeit. anorg. Chem.*, 44 (1905), 43.

The stibinic acids readily yield nitro derivatives in which the nitro group occupies the meta position with respect to the stibinic acid group, provided, of course, that there are not other groups present which hinder substitution in this position. Also, labile groups attached to the benzene ring may be replaced quite easily without affecting the remainder of the molecule.



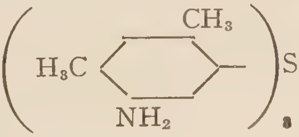
The aryl stibinic acids may be reduced either to stibinous oxides, or derivatives of these oxides—stibinous chlorides—or to stibino compounds depending upon the reducing agent which is employed. Stannous chloride produces aryl stibinous chlorides from which the oxides may be obtained by the action of alkali; the oxides may also be obtained by reducing the stibinic acids with sulfur dioxide and hydrogen iodide. When sodium hydrosulfite is used as the reducing agent, the stibinic acids are converted directly into stibino compounds. These reductions must be controlled much more carefully than is necessary in the case of the arsenicals on account of the ease with which the antimonial group is eliminated from the aromatic nucleus.

When nitro groups are present in the stibinic acid, an additional point of attack is presented for reduction. Stannous chloride and sodium hydrosulfite in excess reduce both groups; attempts to reduce m-nitrophenylstibinic acid to the amino acid by means of sodium amalgam in methyl alcohol or by use of ammonium sulfide failed.[25] To carry out this reaction, it was found necessary to reduce the nitro acid to m-aminophenylstibinous oxide and oxidize this to the stibinic acid. By carefully treating 3-nitro-4-hydroxyphenylstibinic acid with sodium hydrosulfite it is possible to limit the reduction to the nitro group; 3-amino-4-hydroxyphenylstibinic

[25] May: *J. Chem. Soc.*, **101** (1912), 1033.

acid is obtained.[26] o-Nitrophenylstibinic acid is reduced to the corresponding amino acid by either ferrous hydroxide or titanous chloride.[27]

The tendency to decompose with elimination of the antimonial group exists amongst the stibinic acids, but not to as great an extent as in the stibinous series; the substituents and the positions which they occupy in the aromatic nucleus affect the stability of the substances very greatly. Thus, while phenyl and m-aminophenylstibinic acids are not altered by heating with hydrochloric acid, the p-amino acid decomposes when heated for only a short time with dilute hydrochloric acid; the latter stibinic acid, even when kept in the solid state, frequently decomposes sufficiently to yield the odor of aniline. The influence of hydrochloric acid on the decomposition of certain antimonials was previously mentioned in discussing the conversion of triaryl stibines into diarylstibinous chlorides. The influence of the position of substituent groups, and the disrupting effect of hydrochloric acid explain the observation that while the antimony in tri-p-aminophenylstibine is eliminated during the benzoylation of the amino group with benzoyl chloride, tri-5-benzoyl-amino-tri-m-xylylstibine may be obtained from tri-5-amino-tri-m-xylylstibine—



Sb—and benzoyl chloride.

B. Aromatic Stibino Compounds.

At present the aromatic stibino compounds can be prepared by only one method, i.e., reduction of aryl stibinic acids or their primary reduction products, the aryl stibinous oxides or chlorides,[28] with sodium hydrosulfite, or in the case of the stibinous compounds, with sodium hypophosphite. The experimental conditions under which these reductions are made must be carefully adjusted due to the ease with which antimony is eliminated from organic combination. When decomposition occurs during the reaction, complex, dark colored, organic antimonials are obtained.

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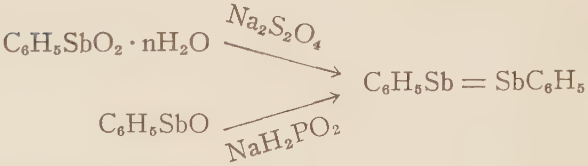
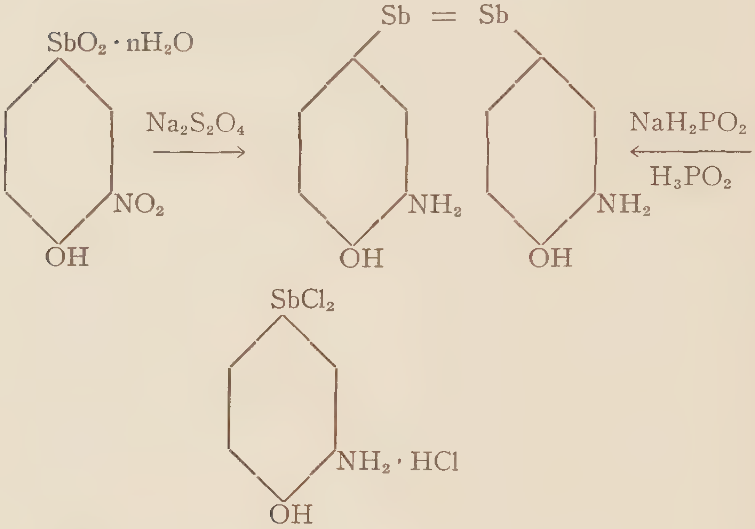
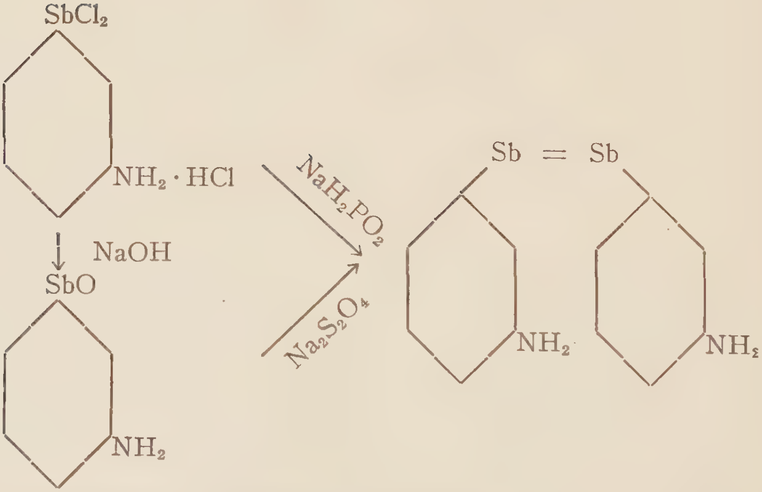
[26] Ger. Pat. 270,488.
[27] Macallum: *J. Soc. Chem. Ind.*, **42** (1923), 468T.
[28] Ger. Pat. 268,451.



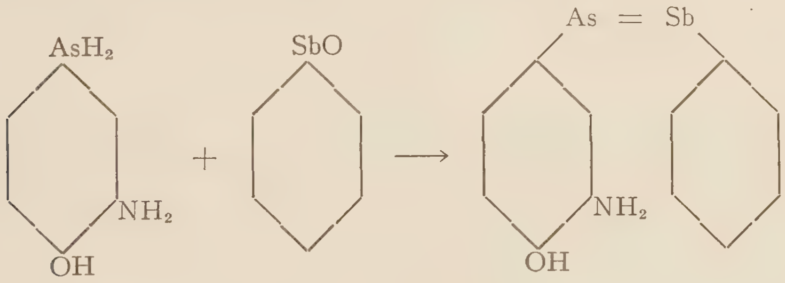
$$C_6H_5SbO_2 \cdot nH_2O \xrightarrow{Na_2S_2O_4} C_6H_5Sb = SbC_6H_5 \xleftarrow{NaH_2PO_2} C_6H_5SbO$$

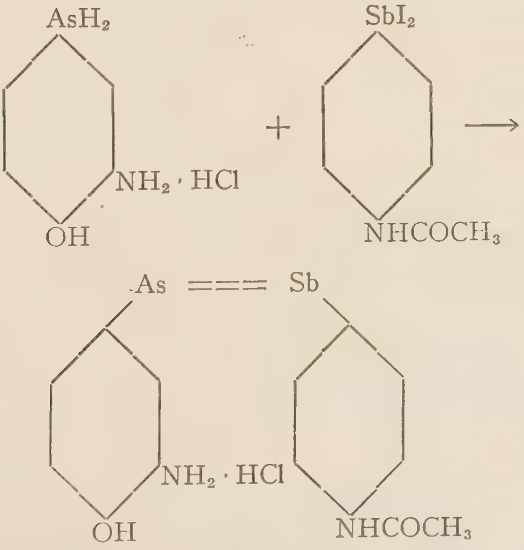




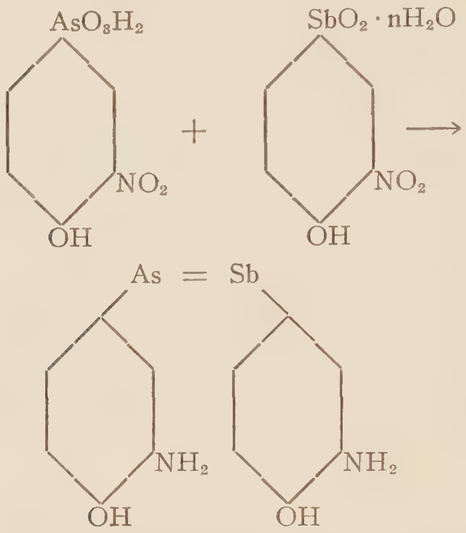
The aryl stibino compounds are amorphous, dark brown solids, which are insoluble in water unless groups are present which permit the formation of salts. They are extremely sensitive to oxidation; concentrated nitric acid oxidizes them violently, and stibinobenzene is somewhat inflammable in the air. Hydrochloric acid exerts a disrupting influence on the stibino compounds; some of the antimony is freed from organic combination and deeply colored products are formed. It is necessary, therefore, to use an excess of sodium hypophosphite in reducing aryl stibinous chlorides to stibino compounds in order that no free hydrochloric acid shall be present. In the presence of alkali, hydrogen peroxide oxidizes compounds of this type to aryl stibinic acids.

Mixed arseno-stibino compounds may be obtained either by condensing a primary aryl arsine with an arylstibinous oxide or halide in methyl alcohol solution,[29] or by reduction of a mixture of aryl arsonic and stibinic acids with sodium hydrosulfite.[30]

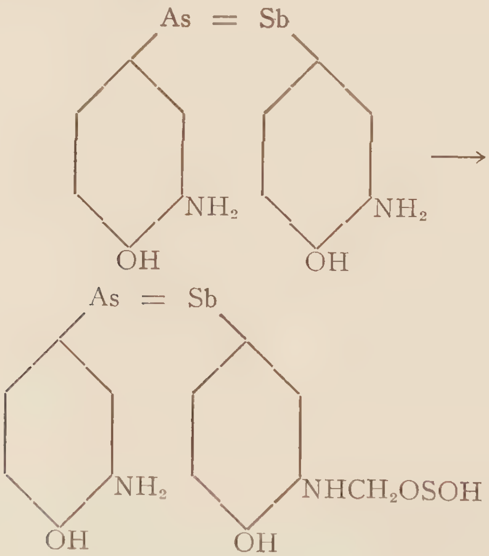




[29a] Ehrlich and Karrer: *Ber.*, 46 (1913), 3564.
[b] Ger. Pat. 269,743; 269,744.
[30] U. S. Pat. (a) 1,111,821; (b) 1,422,294.



Mixed compounds of this type are yellow-brown amorphous solids which are somewhat more stable than the stibino compounds; and which, in the absence of salt forming groups, are insoluble in water. Amino aryl arseno-stibino compounds like the arseno compounds yield N-methylene sulfinic acid derivatives when treated with sodium formaldehyde-sulfoxylate,[30b]



C. Secondary Aromatic Stibinic Acids.

Preparation.

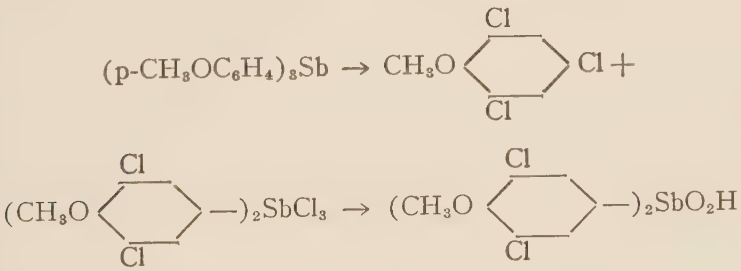
1. The secondary aryl stibinic acids may be prepared from the diaryl stibinous chlorides by the addition of chlorine and hydrolysis of the stibinic chloride which is formed,[31] or by alkaline oxidation of a diarylstibinous oxide with hydrogen peroxide.

$$\mathrm{Ar_2SbCl} \rightarrow \mathrm{Ar_2SbCl_3} \rightarrow \mathrm{Ar_2SbO_2H}$$

2. In the dearylation of tertiary aryl stibines by oxidation with hydrogen peroxide in the presence of alkali, diaryl stibinic acids are formed.[32]

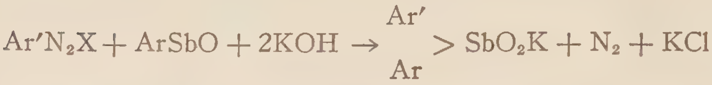
$$(\mathrm{p\text{-}CH_3CONHC_6H_4})_3\mathrm{Sb} \xrightarrow[\mathrm{NaOH}]{\mathrm{H_2O_2}} (\mathrm{p\text{-}CH_3CONHC_6H_4})_2\mathrm{SbO_2Na} + \mathrm{C_6H_5NHCOCH_3}$$

A similar but more complex reaction takes place when tri-p-anisylstibine is treated with chlorine.[33]



3. If the antimony trioxide which is used in the diazo synthesis of aryl stibinic acids is replaced by a primary aryl stibinous oxide, the resulting acid is a secondary aryl stibinic acid. Obviously, this method may be employed in preparing symmetrical and unsymmetrical secondary acids, whereas the methods mentioned above produce only the symmetrical compounds. As the primary aryl stibinous oxides are easily obtained from the stibinic acids, the diazo-reaction serves as a very convenient means of obtaining the secondary aryl stibinic acids.[34]

[31] Michaelis and Reese: *Ann.*, **233** (1886), 39.
[32] Schmidt: *Ann.*, **429** (1922), 125.
[33] Löloff: *Ber.*, **30** (1897), 2835.
[34] Ref. 5, p. 233.

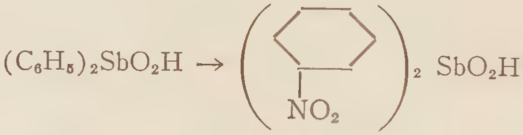


$$\mathrm{Ar'N_2X + ArSbO + 2KOH \rightarrow \begin{matrix}Ar'\\ \\ Ar\end{matrix} > SbO_2K + N_2 + KCl}$$

Properties. Although the secondary acids appear to be complex association products, to some extent at least, they differ noticeably in this respect from the primary stibinic acids, and their behavior toward alkali does not permit any definite conclusions to be made regarding the degree of association. Moreover, the manner in which the acids of this series are precipitated materially affects their solubility in alkali. For example, diphenylstibinic acid, in the form obtained by treating the stibinic chloride with ammonia, is insoluble in ammonia and sodium carbonate, but soluble in caustic soda.[35] If, however, a solution of the chloride in sodium hydroxide is acidified with acetic acid, the resulting diphenylstibinic acid is soluble in ammonium hydroxide and sodium carbonate as well as in sodium hydroxide. It has been suggested that these differences are results of existence of this substance in different degrees of hydration.[36] Also, the stibinic acid which is obtained by treating a hydrochloric acid solution of m-diamino-diphenylstibinic chloride with sodium acetate is, when dried, insoluble in alkali; but when excess caustic soda is added to such a hydrochloric acid solution, a solution of the stibinate is obtained.[37]

The secondary acids also differ from the primary acids in their behavior to hydrochloric acid and ammonium chloride. Diphenylstibinic acid is not only insoluble in concentrated hydrochloric acid, but when dissolved in hot dilute hydrochloric acid, it does not yield a double salt with ammonium chloride; pyridine hydrochloride does, however, precipitate the diphenylstibinic chloride as a double salt.[38]

The secondary acids may be nitrated easily, and as in the primary series, the nitro group enters in the meta position to the antimonial group.



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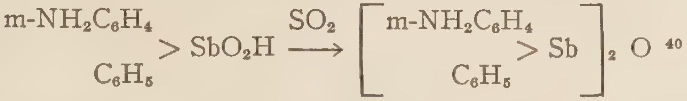
[35a] Ref. 31.
[b] Michaelis and Günther: *Ber.*, 44 (1911), 2319.
[36] Ref. 11, p. 2296.
[37] Ref. 5, p. 241.
[38] Ref. 5, p. 237.
[39] Ref. 11, p. 2293.

Reducing agents convert the acids into stibinous oxides, and when nitro groups are present, they are also reduced.



$$\begin{matrix} m\text{-}NH_2C_6H_4 \\ C_6H_5 \end{matrix} > SbO_2H \xrightarrow{SO_2} \left[\begin{matrix} m\text{-}NH_2C_6H_4 \\ C_6H_5 \end{matrix} > Sb \right]_2 O$$ [40]

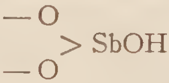
$$(m\text{-}NO_2C_6H_4)_2SbO_2H \xrightarrow[\substack{\text{or} \\ Zn + NH_4Cl}]{Sn + HCl} (m\text{-}NH_2C_6H_4)_2SbOH$$ [41]

Mercuric chloride decomposes diphenylstibinic acid in methyl-alcoholic hydrochloric acid with the formation of phenylmercuric chloride and antimony trichloride,[42] thereby, illustrating again the rupturing of the C-Sb bond.

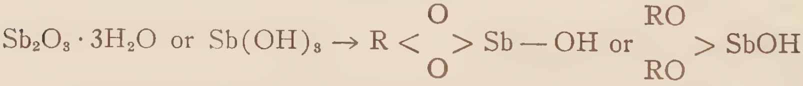
[40] Ger. Pat. 269,206.
[41] Morgan and Micklethwait: *Chem. Soc. Proc.*, **28** (1912), 20.
[42] Michaelis and Reese: *Ann.*, **233** (1886), 39.

Chapter 5.

Antimonyl Compounds

In addition to the strictly organic antimonials, there are a large number of organic derivatives of antimony in which the antimony, instead of being bound directly to a carbon atom, is separated from the latter by an atom of oxygen. The term antimonyl compounds which has been applied to this class of substances is, therefore, indicative of the presence of an $-\mathrm{O}-\mathrm{Sb}=\mathrm{O}$ or  $\begin{array}{l}-\mathrm{O}\\ -\mathrm{O}\end{array}\!>\mathrm{SbOH}$ group. Evidently the organic antimonyl compounds are derivatives of hydrated antimonious oxide, in which all or part of the hydrogen has been replaced by an organic radical R.[1]

$\mathrm{Sb_2O_3\cdot H_2O}$ or $\mathrm{HOSb}=\mathrm{O}\rightarrow\mathrm{ROSb}=\mathrm{O}$



$\mathrm{Sb_2O_3\cdot 3H_2O}$ or $\mathrm{Sb(OH)_3}\rightarrow \mathrm{R}<\begin{array}{c}\mathrm{O}\\ \mathrm{O}\end{array}>\mathrm{Sb}-\mathrm{OH}$ or $\begin{array}{c}\mathrm{RO}\\ \mathrm{RO}\end{array}>\mathrm{SbOH}$

It is only a very short step from the latter type of compound to one in which all the hydrogen atoms of the hydrated oxide are replaced by organic groups, $\mathrm{(RO)_3Sb}$. The existence of sulfur analogues of oxygen compounds, which is quite a common occurrence, has been found to extend into the field of organic antimonyl compounds. Thus, antimonial derivatives of aliphatic sulfur compounds are known which contain the $\equiv\mathrm{C}-\mathrm{S}-\mathrm{Sb}<$ group. Due to the difficulty of drawing a sharp line of demarcation between the compounds which have been commonly termed antimonyls and the $\mathrm{(RO)_3Sb}$ and $\mathrm{RSSb}<$ compounds, it seems advisable to include compounds of the latter types in this division.

A. The Antimonyl Derivatives of Aliphatic Hydroxy Acids.

The original and most widely known member of this class of antimonials is tartar emetic—the antimonyl derivative of potassium bitartrate, but the field has been extended greatly in two directions; antimonyl compounds have been prepared from a number of bitartrates other than that of potassium and from salts of acids other than tartaric acid. Whereas the type of base which is combined with an hydroxy acid has very little influence on the formation of antimonyl derivatives, the structure of the organic acid is of utmost importance and only those acids which contain an α hydroxy group may be used. If this requirement is fulfilled the substance will react with antimony trioxide irrespective of the structure of the remainder of the molecule, but the speed of reaction and the isolability of the product are materially influenced by the other groups present in the molecule. The hydroxy acids which have been used include mono-hydroxy-mono-basic acids, mono-hydroxy-poly-basic acids, and poly-hydroxy-poly-basic acids. It is rather odd that, of all the acids which have been studied, tartaric acid—the first one which was used in this reaction—is the one which reacts most smoothly and which yields the most easily isolable products. In all reactions of this type, the speed of reaction is greatly accelerated by the use of freshly prepared antimony oxide.

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[1] As used here R signifies an organic group and not merely an alkyl group.

Although antimony oxide reacts with many hydroxy acids when the latter are in aqueous solution, this reaction is not practicable for the preparation of antimonyl compounds due to the low rate at which it proceeds, to the difficulty of isolating crystalline reaction products, and to the variability of the composition of the products. The reaction seems to be capable of yielding any one of a series of products depending upon the nature of the antimony oxide, the proportion of the reactants, the experimental conditions, and the manner in which the products are isolated. Investigations in this field have dealt mainly with the reaction between antimony oxide and tartaric acid. In order to secure antimonyl tartaric acid, i.e. the acid corresponding to potassium antimonyl tartrate, products must be prepared containing tartaric acid and antimony in the ratio of 1 : 1. When an excess of antimony oxide, which has been prepared by decomposition of antimony trichloride in hot water and ammonium hydroxide is refluxed with tartaric acid, the reaction proceeds slowly, but the amount of oxide which dissolves is never sufficient to yield a solution containing the reactants in the ratio stipulated for complete reaction.[2] When the experiment is carried out in the cold, the rate of reaction is lower, but the quantity of

[2] Guntz: *Compt. rend.*, **104** (1887), 805.

oxide which dissolves is larger; it is still too small, however, to satisfy the requirements of the above ratio. If, instead of decomposing the antimony trichloride in hot water, the oxide is prepared at room temperature, it is obtained in a form which is more active and probably more extensively hydrated than that which is obtained at the higher temperature. When this form of the oxide is treated with a cold aqueous solution of tartaric acid,[3] the ratio of tartaric acid to antimony in the resulting solution is nearer 1 : 1 than when the reaction mixture is refluxed; after one month the ratio is 1.76 : 1.[4] Upon evaporation of solutions prepared in this way, sirups are obtained which, after standing for a long time, yield crystalline masses which are either mixtures of antimonyl tartaric acid and free tartaric acid or compounds in which several tartaric acid residues are attached to one antimony atom.[5] Acetone extracts tartaric acid from the material, and the residue analyzes for $SbO(C_4H_5O_6) \cdot H_2O$ [6] or antimonyl tartaric acid. When this substance, prepared from the active antimony oxide and a cold solution of tartaric acid, is treated with sufficient potassium carbonate to neutralize one carboxyl group, tartar emetic is obtained.[7] Baudran also states that a di-antimonyl tartaric acid $(SbO)_2C_4H_4O_6$ can easily be obtained in a similar way and that it reacts with potassium tartrate to form tartar emetic. In view of the facts that the reactants combine extremely slowly, that the ratio of acid to antimony approaches unity, but does not reach it, and that Baudran gives neither the details of his experiment nor analyses of the di-antimonyl compound, the existence of such a substance is rather improbable.

If an aqueous solution of tartaric acid is refluxed with a quantity of antimony oxide which is less than that required to saturate it, evaporation yields a crystalline product instead of a sirup; as the proportion of oxide is decreased, the crystallizing power of the residue increases.[8] The isolation of definite compounds in this way is very difficult, and when aqueous solutions of the crystalline masses are treated with alcohol the resulting precipitates are always richer in antimony than the original materials. Clarke and Evans suggested that there are a series of compounds formed by the action of tartaric acid on antimony oxide and that one may be converted into another when precipitated from water solution by alcohol. It seems quite probable, however, that some of their products were mixtures from which precipitation with alcohol removed the excess tartaric acid.

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[3] Dextro and racemic tartaric acids behave similarly in these experiments.

[4] Blanchetière: *Bull. soc. chim.*, (4) **27** (1920), 480.

[5] Péligot: *Ann. Chim. Phys.*, [3] **20** (1847), 283, was the first investigator to secure crystalline material from the sirup obtained by evaporation of solutions prepared by refluxing aqueous tartaric acid with antimony oxide.

[6] Ref. 4, p. 486.

[7] Baudran: *Ann. Chim. Phys.*, [7] **19** (1900), 536.

[8] Clarke and Evans: *Amer. Chem. J.*, **5** (1883-4), 241; *Ber.*, **16** (1883), 2379.

A modification of this reaction involves the aeration of a suspension of finely divided antimony in an aqueous solution of an hydroxy acid;[9] the antimony is first converted into the oxide which then reacts with the acid. As in the cases described above, the reaction is very slow, and the ratio of acid to antimony in the solution never approaches very close to that required for complete conversion of the acid into an antimonyl derivative.

Preparation of Antimonyl Compounds. Obviously the antimonials of this class could not be prepared with any degree of success by the methods outlined above. If, instead of using the free hydroxy acids, their potassium salts are employed, the antimony oxide, if freshly prepared, dissolves rapidly during refluxing, and the antimonyl derivatives may be obtained from the filtered solution either by evaporation or by precipitation with alcohol. In those instances where the product is unstable and decomposes in hot solutions after the excess of antimony oxide has been removed, the evaporation must be carried out at low temperatures. If the product is sufficiently stable it may be purified by recrystallization from water or dilute alcohol. When derivatives of polybasic acids are being prepared, the primary salt of the acid should be used; although potassium bitartrate reacts readily with antimony oxide, Rochelle salt—sodium potassium tartrate—does not. Also, monobasic acids should be treated with only half a molecular equivalent of alkali in order to secure the most satisfactory results. In addition to tartaric acid, glycollic, lactic, α hydroxybutyric, citric, malic and mucic acids may be used in this reaction, but definite products have not been isolated from the α hydroxybutyric acids.

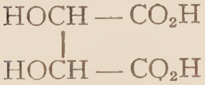
The complexity of the products is quite variable and depends

[9a] Moritz: *Chem. Ztg.*, 26 (1902), 401.

[b] Moritz and Schneider: *Zeit. physik. Chem.*, 41 (1902), 129; *Zeit. angew. Chem.*, 16 (1903), 34.

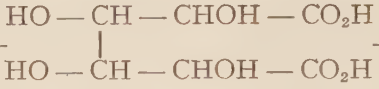
[c] Jordis: *Chem. Ztg.*, 26 (1902), 632.

upon the structure of the hydroxy acid which is used.[10] When the acid contains two sets of α hydroxyl-carboxyl groups as in tartaric—



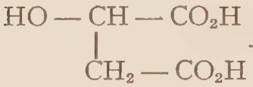
$$\begin{array}{l} \mathrm{HOCH-CO_2H} \\ \ \ \ \ | \\ \mathrm{HOCH-CO_2H} \end{array}$$

—and mucic—



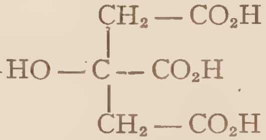
$$\begin{array}{l} \mathrm{HO-CH-CHOH-CO_2H} \\ \qquad\ | \\ \mathrm{HO-CH-CHOH-CO_2H} \end{array}$$

— acids, the antimonyl derivative contains only one acid residue per antimonyl group, and the composition of the substance is comparatively simple, e.g. potassium antimonyl tartrate—$(SbO)(C_4H_4O_6K)$—and potassium antimonyl mucate—$(SbO)(C_6H_8O_8K)$. When, however, only one set of α hydroxyl-carboxyl groups is present as in malic—



$$\begin{array}{l} \mathrm{HO-CH-CO_2H} \\ \qquad\ \ | \\ \qquad\ \mathrm{CH_2-CO_2H} \end{array}$$

—and citric—



$$\begin{array}{l} \qquad\quad\ \mathrm{CH_2-CO_2H} \\ \qquad\quad\ \ | \\ \mathrm{HO-C-CO_2H} \\ \qquad\quad\ \ | \\ \qquad\quad\ \mathrm{CH_2-CO_2H} \end{array}$$

— acids, the products are far more complex and contain two acid residues per antimonyl group.[11] An additional factor which influences the complexity of the reaction products is the formation of double salts. Thus, when potassium acid mucate is treated with antimonyl trioxide, the product isolated is a double salt of potassium antimonyl mucate and potassium acid mucate—$2SbO(C_6H_8O_8K) \cdot C_6H_9O_8K$—from which the simple antimonyl compound may be secured by repeated recrystallization from water.

The antimonyl compounds, the preparation of which has just been discussed, are analogues of tartar emetic in which tartaric acid is replaced by other hydroxy acids; the field has been extended still further by the use of salts other than the potassium salts. The sodium and ammonium acid salts of nearly all of the above acids have been converted into antimonyl derivatives, but owing to the difficulties encountered in isolating definite products and the complexity of many of the derivatives which are obtained when acids other than tartaric acid are used, most of the work with other bases has been done with the tartrates. When it is considered that the structure of tartar emetic—the least complex and the most readily obtainable of all the antimonyl compounds—is still an unsettled question, the use of the tartrates, instead of the salts of

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[10a] Henderson and Prentice: *J. Chem. Soc.*, 67 (1895), 1030.
[b] Henderson and Barr, *Ibid.*, 69 (1896), 1451.
[11] The structure of all of these substances will be discussed later.

acids which yield complex antimonyl derivatives, for the study of compounds in which the potassium is replaced by other bases can be easily understood. The variety of bases which have been successfully substituted for potassium is very great and includes not only inorganic bases but a large number of organic derivatives of ammonia, e.g. alkyl amines, anilines, simple heterocyclic organic nitrogen compounds, and alkaloids; alkyl and sulfonium antimonyl tartrates have also been prepared.

The customary method of preparing this type of antimonyl tartrate has been identical with that used for tartar emetic; the acid tartrate is refluxed with antimony oxide. To obtain successful results, it is essential to have the tartaric acid present as the acid tartrate and to carry the reaction with antimony oxide to the point where the ratio of antimony to tartrate equals unity. Frequently, the products obtained by this method are difficultly crystallizable sirups, and the solids obtained from them do not possess the desired composition. Such results are due to failure to satisfy the requirements stated above. A far more convenient and successful method of preparing these compounds is to convert pure tartar emetic, by the addition of barium chloride, into barium antimonyl tartrate, which is then treated with the calculated quantity of the sulfate of the base in question.[12] After removal of the barium sulfate, the filtrate contains the desired antimonyl tartrate which can easily be isolated by evaporation to crystallization or precipitation with alcohol.

Ethyl antimonyl tartrate was originally prepared by heating ethyl tartrate in a sealed tube with antimony oxide,[13] but a far superior method is to reflux silver antimonyl tartrate, which is readily obtainable from tartar emetic and silver nitrate, with ethyl iodide in absolute alcohol. The product is extracted from the alcohol insoluble material with water and isolated by evaporation of the extract at a low temperature.[14a] Similarly, the complex substituted ammonium antimonyl tartrates may be prepared by treating silver emetic with the amine hydrochloride, e.g. from apothesine hydrochloride, apothesine antimonyl tartrate may be obtained.[14b]

Properties. The antimonyl compounds are white, crystalline solids which are insoluble in alcohol and which vary greatly in

[12] Clarke: *Ber.*, **15** (1882), 1540.
[13] Thomsen and Cushny: *Proc. Roy. Soc. London.*, [B] **82** (1910), 249.
[14a] Brahmachari: *Indian J. Med. Research,* **11** (1923), 196.
[14b] *Ibid.*, **11** (1923), 408.

the extent to which they dissolve in water; some are very soluble and others dissolve only slightly; their behavior in this respect is controlled largely by the nature of the base which has been used. Examples illustrating the range over which the solubility may vary have been selected from the derivatives of tartaric acid—Table IV.

TABLE IV

Solubility of Antimonyl Tartrates

	Quantity Dissolved by 100 c.c. of Water at 18°
Lithium antimonyl tartrate[15]	180 g.
Barium antimonyl tartrate	Very small
Butylamine antimonyl tartrate[15]	238
Quinidine antimonyl tartrate[15]	0.31

The aqueous solutions of these substances are acidic, but the degree of acidity, like the solubility in water, is decidedly variable and depends largely upon the basic component of the compound, e.g. one per cent solutions of benzylamine antimonyl tartrate and acetyl-p-phenylenediamine antimonyl tartrate[16] possess pH values of 5 and 2 respectively.

The usual metathetical reactions of salts may be carried out with these compounds:

$$2SbO \cdot C_4H_4O_6 \cdot K + BaCl_2 \rightarrow (SbO \cdot C_4H_4O_6)_2Ba + 2KCl$$

$$SbO \cdot C_4H_4O_6 \cdot K + AgNO_3 \rightarrow SbO \cdot C_4H_4O_6 \cdot Ag + KNO_3$$

$$(SbO \cdot C_4H_4O_6)_2Ba + (C_6H_5NH_3)_2SO_4 \rightarrow 2SbO \cdot C_4H_4O_6 \cdot NH_3C_6H_5 + BaSO_4$$

$$SbO \cdot C_4H_4O_6 \cdot Ag + C_2H_5I \rightarrow SbO \cdot C_4H_4O_6 \cdot C_2H_5 + AgI$$

In this way cadmium, zinc, iron, and strontium antimonyl tartrates may be prepared.

The antimonyl group is not held very firmly in this type of compound, and great care must be exercised during manipulation in order to avoid decomposition. In some instances the stability is so slight that even during evaporation of an aqueous solution on a steam bath antimony oxide precipitates; however, all antimonyl compounds of this type are decomposed by strong acids and alkalies with the elimination of antimony oxide. The decomposition is never complete and varies with the quantity of the reagent added, the concentration of the solution, and the temperature. For example, when a dilute solution of tartar emetic is treated with varying amounts of hydrochloric acid or caustic potash, the proportion of the antimony which is precipitated varies[17]—Table V..

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[15] Fargher and Gray: *J. Pharm. and Exper. Therap.*, 18 (1921), 348, 349, 351.

[16] Private communication from Christiansen and Norton.

TABLE V

DECOMPOSITION OF SOLUTIONS OF TARTAR EMETIC

Precipitant		*Per Cent of Total Antimony which Precipitates*
HCl	1 equiv.	10.5
	16	58.0
KOH	1	23.0
	2	96.0
	16	Precipitate redissolves

The extent to which decomposition occurs is decreased by diluting the solution or lowering the temperature; also, sulfuric acid precipitates less of the antimony than hydrochloric acid does. Guntz attributed the solution of the precipitate in a large excess of caustic potash to the formation of potassium antimonite, but a polarimetric study of the new solution has led to the suggestion that a new antimony derivative of potassium tartrate is formed.[18]

By carefully controlling the conditions under which these salts are acidified, it is possible to obtain solutions of the free antimonyl acids; if a suspension of barium antimonyl tartrate in cold water is treated with an *exactly* equivalent amount of cold sulfuric acid, the filtrate from the barium sulfate contains antimonyl tartaric acid.[19] This solution reacts with potassium and barium carbonates regenerating tartar emetic and barium antimonyl tartrate. The acid is very unstable and can not be isolated; even very gentle warming or a very slight quantity of sulfuric acid causes partial decomposition with the precipitation of antimony oxide. However, complete decomposition is never secured even by refluxing the solution. In a similar manner, solutions of antimonyl citric acid may be prepared, but in this case the compound may be isolated in the crystalline condition,[20] $HOSb(C_6H_7O_7)_2$; when treated with the calculated quantity of potassium carbonate, the antimonyl acid is reconverted into the original potassium antimonyl citrate. Mineral acids cause immediate decomposition.

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[17] Guntz: *Compt. rend.*, 102 (1886), 1472.

[18a] Grossmann: *Zeit. physik. Chem.*, 57 (1907), 533.

[b] Darmois: *Compt. rend.*, 177 (1923), 49.

[19] Clarke and Stallo: *Amer. Chem. J.*, 2 (1880-1), 319; *Ber.*, 13 (1880), 1787.

[20] Ref. 10a, p. 1032.

Just as carefully controlled acidification of the barium salts yields solutions of the free antimonyl acids, without the elimination of antimony oxide, the solutions of the antimonyl salts may be neutralized with alkalies without immediate precipitation. When cold solutions of sodium carbonate and tartar emetic are mixed, the solution remains perfectly clear until it has stood for some time; the precipitation is hastened by warming.[21] All alkaline salts behave similarly, and the amount of antimony oxide precipitated by them is a function of the time, temperature, and quantity of reagent; the decomposition is never complete, however.[22]

$$2SbOC_4H_4O_6K + 2CH_3CO_2Na \rightarrow 2C_4H_4O_6 \cdot K \cdot Na + Sb_2O_3 \cdot H_2O + 2CH_3CO_2H$$

Hydrogen sulfide converts the antimony in all compounds of this type into antimony sulfide, but unless the solution has been acidified the latter remains in colloidal solution. Such a solution—prepared from a dilute solution of tartar emetic is orange colored, clear, and very stable; boiling does not cause coagulation. Upon dialysis the solution gradually becomes fluorescent, and after several weeks the sulfide starts to precipitate. The solution is not a true one, but contains excessively minute particles;[23] the addition of electrolytes causes immediate coagulation.

Electrolysis decomposes the antimonyl compounds with the deposition of antimony at the cathode. Hemmelmeyer[24] electrolyzed solutions of tartar emetic using platinum electrodes and found that the deposit of antimony on the cathode was contaminated with antimony trioxide in variable amounts, depending upon the concentration of the solution and the current density. None of the suboxide, Sb_2O_5, reported by Marchand[25] could be detected.

Solutions of these antimonials reduce iodine, and tartar emetic has been found to reduce mercuric chloride to mercurous chloride and potassium chromate to a brown basic chromium salt.

Studies of the physical properties of solutions of tartar emetic show that the antimonyl compounds are still less stable than the experiments in which antimony oxide is precipitated indicate. The specific rotation of tartar emetic in aqueous solution depends somewhat upon the nature of reagents used in preparing it. Although the products obtained from either "natural" or "artificial" [26] potassium bitartrate and antimony oxide, which has been secured by hydrolysis of the trichloride either in hot or cold solution, appear to be identical in all cases, an examination of the optical rotation caused by their solutions shows that they differ physically.[27]

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[21] Long and Sauer: *Chem. News*, **63** (1891), 269.

[22] Long: *J. Amer. Chem. Soc.*, **17** (1895), 87.

[23] Picton: *J. Chem. Soc.*, **61** (1892), 142.

[24] Hemmelmeyer: *Monatsch. f. Chem.*, **23** (1902), 262.

[25] Marchand: *J. prakt. Chem.*, **34**, 381.

When alkaline salts, like sodium carbonate or acetate, are added to solutions of tartar emetic no immediate precipitate appears unless heat is applied. However, since a gradual decrease in the specific rotation commences at once, the antimonyl compound begins to decompose as soon as the reagent has been added; the magnitude of the rotation may decrease as much as 60% before precipitation sets in.[28] Only slight diminutions in the optical rotatory power of tartar emetic solutions result when the temperature is raised, or neutral salts are added, or the solution is diluted.[29] The substitution of glycerin for water as a solvent does not affect the specific rotation.[30]

The slight diminution in rotatory power which occurs when aqueous solutions of tartar emetic are heated or diluted indicates that decomposition takes place, although to a very slight extent, even in the absence of other salts; this tendency is also detected in conductivity experiments [29] and in the behavior of aqueous solutions which are allowed to stand for a long time. When a solution of 16 g. of tartar emetic in a liter of water is allowed to stand in a stoppered bottle for 14 months, 3.5% of the substance decomposes with the precipitation of antimony trioxide; simultaneously a small amount of fungus develops.[31] More concentrated solutions are more stable, and no deposition of antimony trioxide is observed over a period of three months.[32] The exclusion of air from solutions of this substance is said to decrease the rate of decomposition.[33] Evidently the separation of antimony oxide from solutions of tartar emetic is a slow process and never represents more than a small proportion of the total antimonyl compound present. Hädrich[34] also mentions the fact that the solutions become cloudy only after a considerable period of standing and that the rate is increased by increasing the dilution. Some antimonyl compounds decompose much more extensively in water solution than tartar emetic does; solutions of the lactate yield precipitates of antimony oxide very readily.[35] Solutions of the analogues of tartar emetic may be stabilized by adding the acid or a salt of the acid from which the substance has been derived.

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[26] Prepared from recrystallized tartaric acid and potassium tartrate which has been obtained from the recrystallized acid; the "artificial" and "natural" forms differ in optical rotatory power.

[27] Baudran: *Ann. Chim. Phys.*, [7] **19** (1900), 536.

[28] Long: *Amer. J. Sci. and Arts.*, [3] **38** (1889), 264; Ref. 21.

[29] Hädrich: *Zeit. physik. Chem.*, **12** (1893), 494. Dilution of aqueous solutions of the boron and arsenic analogues of tartar emetic causes a tremendous decrease in the molecular rotation, indicating that these compounds are decomposed nearly completely in dilute solution.

[30] Long: *J. Amer. Chem. Soc.*, **23** (1901), 813.

[31] Gruener: *Amer. J .Sci.*, [3] 46 (1893), 206.

[32] Christiansen and Norton: *J. Lab. and Clin. Med.*, **9** (1923), 34.

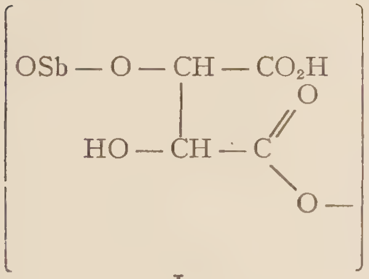
[33] Miller: *J. Sod. Chem. Ind.*, **5** (1886), 464.

Structure. The antimony in the antimonyl compounds is united to an organic residue to form a complex group which possesses a certain amount of stability; in the metathetical reactions of these compounds the complex group acts as a single unit, thereby enabling the conversion of one salt into another, and under the proper conditions the free antimonyl acid may be obtained in which the complex group is still intact, e.g. solutions of antimonyl tartaric acid and crystalline antimonyl citric acid may be secured. The molecular rotation of a solution of tartar emetic is due to the antimonyl tartrate ions, $SbOC_4H_4O_6'$, and since the rotation is much greater than that found for potassium tartrate and does not alter greatly in the absence of acids or bases, the above complex ion must remain unchanged. The arsenyl tartrate ion, $AsOC_4H_4O_6'$, also causes a greater rotation than the tartrate ion, but it decomposes readily and the molecular rotation of potassium arsenyl tartrate rapidly approaches that of potassium tartrate. Other evidence that the complex ion is fairly stable is the absence of antimony ions from a solution of tartar emetic.[36]

When the antimony is precipitated carefully by means of acids[37] or alkalies[38] or by warming a solution of antimonyl tartaric acid,[39] it appears as hydrated antimony oxide. Also, antimonyl tartaric acid can be obtained from tartaric acid and active, i.e. hydrated antimony oxide, by extracting the crude reaction product with acetone.[40] The optical rotation and conductivity studies merely require that the formula of the complex ion shall be such as to in-

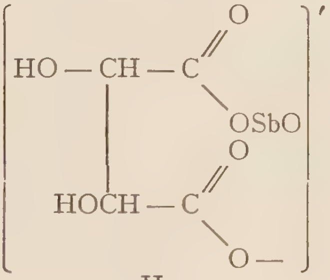
[34] Hädrich: *Zeit. physik. Chem.*, **12** (1893), 494.
[35] Jordis: *Zeit. angew. Chem.*, **15** (1902), 909.
[36] Kahlenberg: *Zeit. physik. Chem.*, **17** (1895), 605.
[37] Guntz: *Compt. rend.*, **102** (1886), 1472.
[38] Long and Sauer: *Chem. News*, **63** (1891), 269.
[39] Clarke and Stallo: *Amer. Chem. J.*, **2** (1880-1), 319; *Ber.*, **13** (1880), 1787.
[40] Ref. 4, p. 486.

dicate the tendency to undergo hydrolysis. The complex ion in tartar emetic, therefore, is one which may be obtained from and converted into tartaric acid and hydrated antimony oxide and could be represented by replacing a hydrogen atom either of the hydroxyl [41] group or the carboxyl group of tartaric acid with an antimonyl group—



I

or



II

In one case the product is an ester of antimonious acid; in the other it is a salt analogous to antimonyl nitrate, $OSb-ONO_2$, in which the antimonyl group plays the rôle of a univalent metal, or it might be considered a basic antimony salt of tartaric acid comparable with antimony oxychloride. Both alkyl and aryl esters of antimonious acid have been prepared by the action of alcohols and phenols on antimony trioxide and have been found to hydrolyze very readily.[42] Also, antimonyl nitrate and sulfate, and antimony oxychloride hydrolyze to form antimony trioxide. Consequently, either of the above formulæ might represent the complex ion.

Compounds of the antimonyl type can only be obtained from α hydroxy acids. Table VI shows the solubility of antimony trioxide in aqueous solutions of aliphatic acids to which sodium carbonate has been added;[43] as antimony trioxide is very insoluble in water, the large amounts dissolved by these solutions must be indicative of reaction. Henderson and Prentice [44] isolated antimonyl derivatives of salts of citric, malic, and mucic acids but failed to get any reaction with acids containing no hydroxyl group. Therefore, in view of the necessity of the presence of an α hydroxyl group either formula I must be correct or else the hydroxyl group acts indirectly

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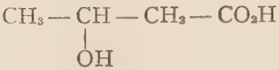
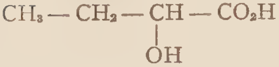
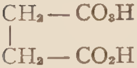
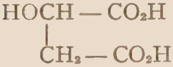
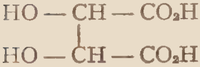
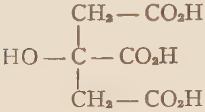
[41] Jungfleisch: *Bull. soc. chim.*, [2] **40** (1883), 98.
[42] Mackey: *J. Chem. Soc.*, **95** (1909), 604.
[43] Moritz and Schneider: *Zeit. physik. Chem.*, **41** (1902), 129.
[44] Henderson and Prentice: *J. Chem. Soc.*, **67** (1895), 1030.

TABLE VI

Acid	*Wt. of Acid* g/1	*Wt. of* Na_2CO_3 g/1	Sb_2O_3 *Dissolved* g/1
 $CH_3-\underset{OH}{\underset{\mid}{CH}}-CH_2-CO_2H$	58	12	1.7
 $CH_3-CH_2-\underset{OH}{\underset{\mid}{CH}}-CO_2H$	98	28	37.0
 $\begin{array}{l} CH_2-CO_3H \\ \mid \\ CH_2-CO_2H \end{array}$	59	23	trace
 $\begin{array}{l} HOCH-CO_2H \\ \quad\mid \\ \quad CH_2-CO_2H \end{array}$	140	36	49
 $\begin{array}{l} HO-CH-CO_2H \\ \qquad\mid \\ HO-CH-CO_2H \end{array}$	72	21	60
 $\begin{array}{l} \qquad CH_2-CO_2H \\ \qquad\mid \\ HO-C-CO_2H \\ \qquad\mid \\ \qquad CH_2-CO_2H \end{array}$	71	25	24

and affects the carboxyl group so that a substance represented by II may form. While an α hydroxyl group increases the strength of an organic acid a β hydroxyl group does not; if the antimonyl group is to become attached to the carboxyl group, any influence increasing the acid character of this group should favor the formation of such a derivative. If the α hydroxyl group is essential only as an activating influence as in formula II other negative substituents, e.g. chlorine atoms, in the α position should act similarly; this is not the case, Table VII.

TABLE VII[45]

THE EFFECT OF α SUBSTITUENTS ON THE REACTION BETWEEN ANTIMONY OXIDE AND ACETIC ACID

Acid	*Normality of Acid Solution* N	Sb_2O_3 *Content when the Acid Solution is Saturated with Oxide* %
CH_3CO_2H	1	0.0016
	20.5	0.58
$ClCH_2CO_2H$	7.4	0.07
Cl_2CHCO_2H	5.5	0.2
Cl_3CCO_2H	5.34	0.1
$HOCH_2CO_2H$	4.88	2.83

Moreover, if the reaction depends upon the increased acidic nature due to the α substituent, it is difficult to see why the addition of a certain amount of alkali should favor the reaction. A 4.88 N solution of glycollic acid to which ½ of an equivalent of caustic potash has been added contains, after saturation, 12.16% Sb_2O_3, and a potassium antimonyl glycollate can be isolated as a double salt with potassium glycollate.[46] It appears, therefore, that the hydroxyl group takes part in the reaction and that these antimonyl compounds are represented by formulæ analogous to I.

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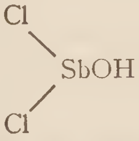
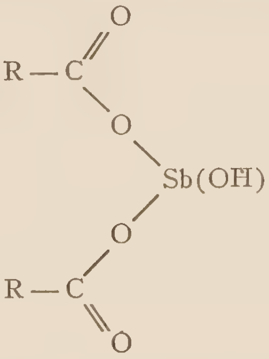
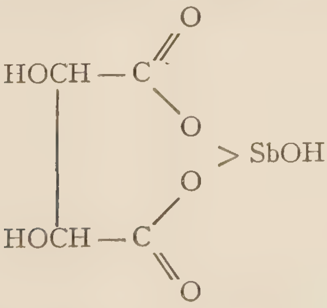
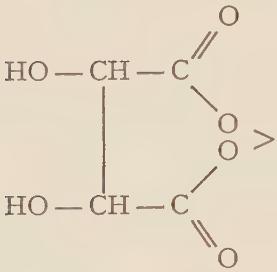
[45] The data in Table VII are part of a paper by Jordis and Meyer: *Zeit. angew. Chem.*, 17 (1904), 169.

Jordis, who accepted neither of the above formulæ, considers that the reaction by which tartar emetic is formed is not peculiar to tartaric acid or other hydroxy acids but is general for all acids.[45] The products are compared to  which is formed by hydrolysis of antimony trichloride and are merely salts of antimonious hydroxide, $Sb(OH)_3$. Thus, the derivatives of monobasic acids are represented by  ; to those of polybasic acids a similar formula is assigned, e.g. antimonyl tartaric acid  ; tartar emetic would be

[46] Ref. 45. No mention is made of any similar behavior of any of the chloroacetic acids.



$>SbOK$.[47] If these substances are to be considered as salts of this type, the ease with which they are formed and their stability should vary in the same direction as the strength of the acid.[48] Inasmuch as antimony oxide possesses basic characteristics, it will react to some extent with organic acids to form salts, and the degree to which this occurs will be greater when a weak acid is replaced by a stronger one. However, as will be seen from Table VIII, the salt formation even with the strong acids is negligible when compared to the reaction which results when an α hydroxy acid is used even though the latter is weaker than some of the other organic acids. Therefore, these antimonyl compounds can not be considered as basic salts of antimonious hydroxide, the formation of which would be a function of the strength of the acid.

TABLE VIII

Acid	*100 x K*	*Normality of Acid Solution* N	Sb_2O_3 *Content of Acid Solution Saturated with* Sb_2O_3 %
CH_3-CO_2H	0.0018	1	0.0016
		20.5	0.58
$CH_3-\underset{\substack{\mid\\ OH}}{CH}-CO_2H$	0.0138	1.21	0.55
		6.7	3.24
$HO-CH_2-CO_2H$	0.0152	4.88	2.83
$ClCH_2CO_2H$	0.155	7.4	0.07
$CH_2(CO_2H)_2$	0.16	0.5	0.018
$\begin{array}{l}CH_2-CO_2H\\ \mid\\ CH_2-CO_2H\end{array}$	0.006	0.5	0.002
$\begin{array}{l}HO-CH-CO_2H\\ \quad\quad\ \mid\\ HO-CH-CO_2H\end{array}$	0.09	0.5	3.9

K is the ionization constant.

Moreover, Jordis' formulation of tartar emetic necessitates that antimonious hydroxide behave simultaneously as a base and an acid, i.e. the antimony is represented as existing both in a salt of tartaric acid and in a potassium antimonite; such simultaneous amphoteric behavior seems rather improbable. Therefore, the interpretation of the formation and structure of the antimonyl compounds which Jordis suggested can not be accepted, and the evidence indicates that the antimony oxide reacts with the hydroxyl group rather than the carboxyl group.

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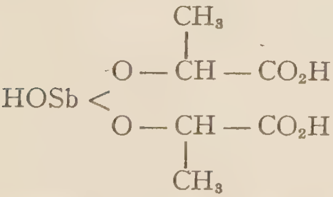
[47] Jordis: *Zeit. angew. Chem.*, **15** (1902), 909.
[48a] Ref. 35.
[b] Jordis: *Zeit. angew. Chem.*, **17** (1904), 41.

The composition of the antimonyl derivatives of citric, malic, tartaric and mucic acids shows that the number of acid residues per atom of antimony in the product is dependent upon the number of hydroxyl groups in the original acid and that the number of carboxyl groups is unessential.[49] Whenever only one hydroxyl group is present in the acid, the product contains two acid residues united to one atom of antimony, whereas when two or more hydroxyl groups are present only one acid residue is combined to each antimony atom.

TABLE IX

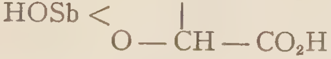
Acid	*No. Hydroxyl Groups*	*No. Carboxyl Groups*	*No. Acid Residues per Atom of Sb in the Product*
Lactic	1	1	2
Malic	1	2	2
Citric	1	3	2
Tartaric	2	2	1
Mucic	4	2	1

This relation, while supporting the ester type of formula, and indicating reaction between the hydrated antimony and the hydroxyl group, led Henderson and Prentice [49] to adopt a modification of formula I, whereby antimonyl lactic and tartaric acids are represented by the formulæ,



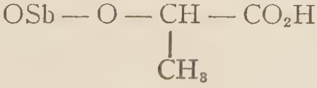
$$HOSb<\begin{array}{l} O-\overset{\displaystyle CH_3}{\overset{|}{C}H}-CO_2H \\ O-\underset{\displaystyle CH_3}{\underset{|}{C}H}-CO_2H \end{array}$$

and



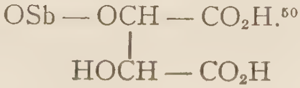
$$HOSb<\begin{array}{l} O-CH-CO_2H \\ \quad\ \ | \\ O-CH-CO_2H \end{array}$$

instead of



$$OSb-O-\underset{\displaystyle CH_3}{\underset{|}{CH}}-CO_2H$$

and



$$OSb-\begin{array}{l} OCH-CO_2H. \\ \quad | \\ HOCH-CO_2H \end{array}$$[50]

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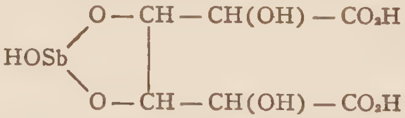
[49] Ref. 10a, p. 1039.

[50] See note on page 90.

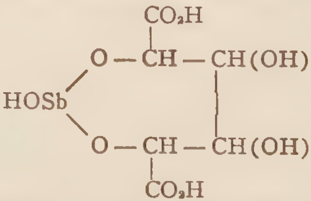
Such a formula also expresses the fact that the antimony oxide takes part in the reaction in its hydrated form and that antimonious hydroxide is the hydrolysis product of antimonyl tartaric acid.[51]

In addition to the evidence given above, there are some physico-chemical data which also support the ester formula for antimonyl compounds. The formation of tartar emetic and antimonyl tartaric acid by the action of antimony oxide on potassium bitartrate and tartaric acid respectively are endothermic reactions in which approximately the same amount of heat is absorbed; [52] if the reaction were one of salt formation involving the replacement of a carboxyl hydrogen by an antimonyl group, the reaction would be exothermic. The neutralization of an aqueous solution of tartar emetic with potassium carbonate evolves an amount of heat equivalent to that calculated for the neutralization of a carboxyl group in such a molecule. The evolution of heat is immediate, whereas the decomposition of the neutralized solution, which is accompanied by the separation of antimony oxide, is a gradual process which is accelerated by warming. The optical rotation experiments also indicate that the hydrolysis of tartar emetic is a very gradual process. Also, if hydrochloric acid, equivalent to the carbonate, is added immediately after neutralization, the solution becomes identical with the original one. Therefore, tartar emetic contains an unneutralized carboxyl group, and the decomposition by alkali is analogous to the saponification of esters.[53] If the decomposition process involved the precipitation of antimony from a salt, the oxide should separate

[50] The derivative of mucic acid is assigned the formula



Ref. 49, but in view of the importance of having the hydroxyl group in the α position, it might be advisable to use the formula

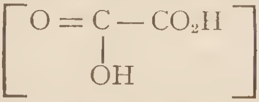


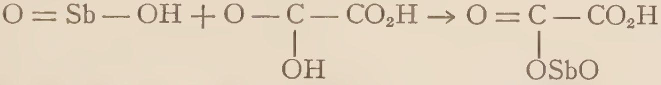
[51] Clarke and Stallo: *Amer. Chem. J.*, 2 (1880-1), 319; *Ber.*, 13 (1880), 1787.

[52] Guntz: *Compt. rend.*, 104 (1887), 699, 850.

[53] Adam: *Compt. rend.*, 118 (1894), 1273.

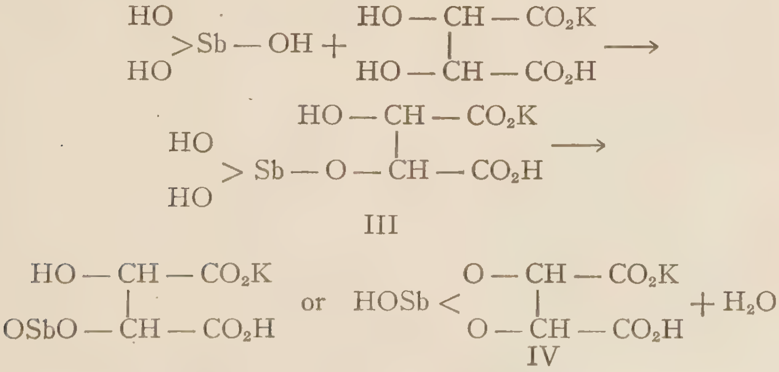
rapidly and completely. The rate of reaction between hydrated antimony oxide and tartaric acid is analogous to that of esterification processes;[54] although fairly rapid at first, the reaction becomes slower and slower and requires some time to complete itself. If salt formation were occurring, it should take place rapidly and be completed in a short time when fresh, hydrated oxide is used.

The formation of antimony derivatives of oxalic acid by treatment with antimony oxide has been omitted from the above discussion but may well be mentioned at this point. As stated above, antimony oxide must react with acids to a certain extent to form salts or basic salts. Oxalic acid is much stronger than any of the other acids which have been discussed ($K \cdot 100 = 10$, cf. Table VIII) and consequently should enter into salt formation reactions with the oxide to a much greater extent than any of the others. However, it also contains an α hydroxyl group  $\left[O{=}\underset{\displaystyle OH}{\underset{|}{C}}{-}CO_2H \right]$, and no matter which point of view—esterification or salt formation—is adopted, the final result is the same.



$$O{=}Sb{-}OH + O{-}\underset{\displaystyle OH}{\underset{|}{C}}{-}CO_2H \rightarrow O{=}\underset{\displaystyle OSbO}{\underset{|}{C}}{-}CO_2H$$

The esterification of the hydroxyl groups of α hydroxy acids appears to be the most satisfactory conception of the formation of these antimonyl compounds, and the resulting formulæ express the properties of the products very well. Tartar emetic may be used as an example.



$$\begin{matrix}HO\\ HO\end{matrix}{>}Sb{-}OH + \begin{matrix}HO{-}CH{-}CO_2K\\ |\\ HO{-}CH{-}CO_2H\end{matrix} \longrightarrow$$

$$\begin{matrix}HO\\ HO\end{matrix}{>}Sb{-}O{-}\begin{matrix}HO{-}CH{-}CO_2K\\ |\\ CH{-}CO_2H\end{matrix} \longrightarrow$$

III

$$\begin{matrix}HO{-}CH{-}CO_2K\\ |\\ OSbO{-}CH{-}CO_2H\end{matrix} \quad \text{or} \quad HOSb{<}\begin{matrix}O{-}CH{-}CO_2K\\ |\\ O{-}CH{-}CO_2H\end{matrix} + H_2O$$

IV

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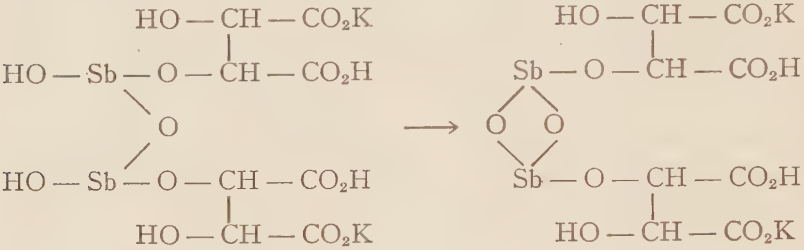
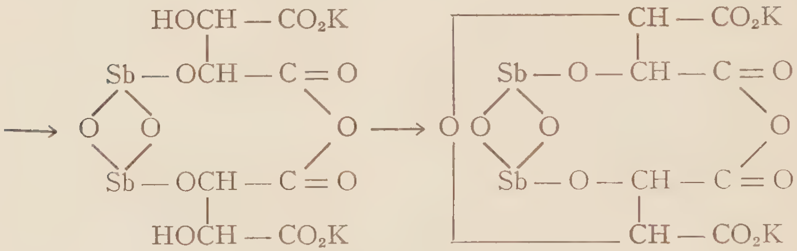
[54] Blanchetière: *Bull. soc. chim.,* [4] 27 (1920), 480.

In the particular instance of tartar emetic, drying at elevated temperatures causes the loss of water of constitution in definite stages. Hale [55] finds that this may be expressed better by representing tartar emetic as V, which is formed from two molecules of III by the loss of a molecule of water, rather than as IV, which is formed from one molecule of III.



V



V

The double formula for tartar emetic has also been suggested by others.[56, 57]

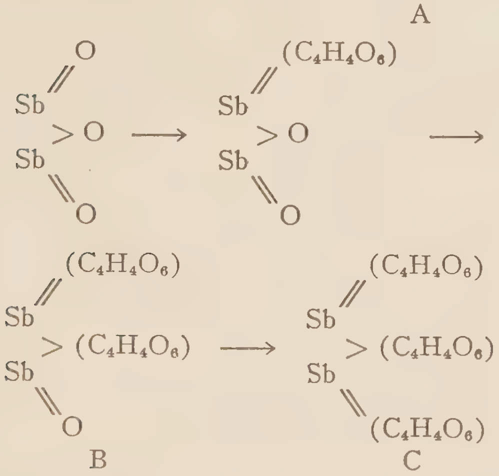
Clarke and Evans,[56] while studying the reaction between antimony oxide and tartaric acid, concluded that a number of products are formed which are derivatives of ortho antimonious acid. They divided these products into two series: derivatives of (a) hydrated and (b) dehydrated antimony trioxide. The following formulæ, in which the manner of union between the antimony atom and the acid residue is omitted, are all that were given, but it seems that the substances were considered to be antimony salts of tartaric acid; only three (A, B, and C) of the possible six were obtained, and the investigations of these three were rather meager.

[55] Hale: *J. Amer. Chem. Soc.*, **24** (1902), 828.

[56] Clarke and Evans: *J. Amer. Chem.*, **5** (1883-4), 241; *Ber.*, **16** (1883), 2379.

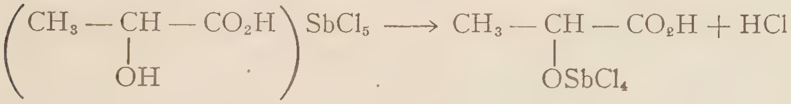
[57] Kahlenberg: *Zeit. physik. Chem.*, **17** (1895), 605.

$$Sb(OH)_3 \rightarrow (HO)_2Sb(C_4H_4O_6 \cdot H) \rightarrow (HO)Sb(C_4H_4O_6 \cdot H)_2 \rightarrow Sb(C_4H_4O_6 \cdot H)_3$$

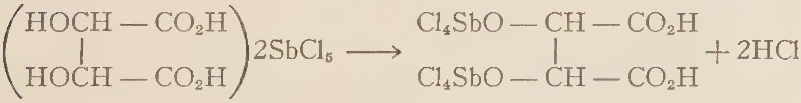


In accordance with their interpretation of these antimony derivatives of tartaric acid as salts, Clarke and his co-workers adopted a similar view with respect to the mode of combination in tartar emetic.

In connection with the application of the ester type of formula to the antimonyl compounds, it is interesting to note that the addition compounds formed by hydroxy acids with antimony pentachloride are very unstable; hydrochloric acid is readily eliminated and a $-SbCl_4$ group replaces the hydroxyl hydrogen atom.[58]



$$\left(CH_3-\underset{\displaystyle OH}{\underset{|}{CH}}-CO_2H\right)SbCl_5 \longrightarrow CH_3-\underset{\displaystyle OSbCl_4}{\underset{|}{CH}}-CO_2H+HCl$$



$$\left(\begin{array}{l}HOCH-CO_2H\\ \quad\;|\\ HOCH-CO_2H\end{array}\right)2SbCl_5 \longrightarrow \begin{array}{l}Cl_4SbO-CH-CO_2H\\ \qquad\qquad|\\ Cl_4SbO-CH-CO_2H\end{array}+2HCl$$

The products of such reactions are crystalline and fairly stable.

B. Alkyl and Aryl Antimonites.

Alkyl and aryl esters of antimony trioxide have been prepared by heating methyl, ethyl, propyl, iso-butyl, amyl, and iso-amyl alcohols, phenol, and ortho, meta, and para-cresols with antimony trioxide in the presence of a dehydrating agent.[59]

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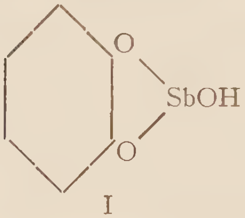
[58] Rosenheim and Loewenstamm: *Ber.*, 35 (1902), 1122.

$$6ROH + Sb_2O_3 \rightarrow 2(RO)_3Sb + 3H_2O$$

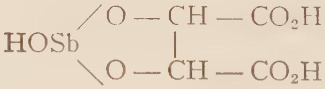
The alkyl antimonites are liquids; the lower members of the series are colorless, but the others are yellow. The boiling point, although only 65° in the case of the methyl compound, increases very rapidly as the size of the alkyl group increases; the propyl and higher esters must be distilled *in vacuo* because decomposition into the alcohol and antimony trioxide occurs at high temperatures. The aryl esters are yellow or brown, high boiling oils which, with the exception of m-tolyl antimonite, may be solidified by cooling slightly below room temperature. These substances are all readily soluble in absolute alcohol, ether, chloroform, and benzene, but hydrolyze readily in water into the original alcohol and antimony trioxide.

C. Antimonyl Derivatives of Polyhydric Phenols.

The aromatic analogues of the antimonyl derivatives of the aliphatic hydroxy acids, cf. antimonyl catechol (I) and antimonyl tartaric acid (II), are readily obtained by the action of hydrated antimony oxide on ortho phenols,[60] but unlike the aliphatic compounds, these compounds, which are acid esters of antimonious acid, are decidedly stable; hydrolysis does not occur even in the presence of aqueous acids or alkalies. The isomeric polyhydric phenols, i.e., the meta and para phenols, also yield antimonites, but the products resemble the normal aryl antimonites, cf. Section B, and hydrolyze readily.[61] Substances of this type have been obtained from catechol, pyrogallol, gallic acid, methyl gallate, and tannic acid.



I



II

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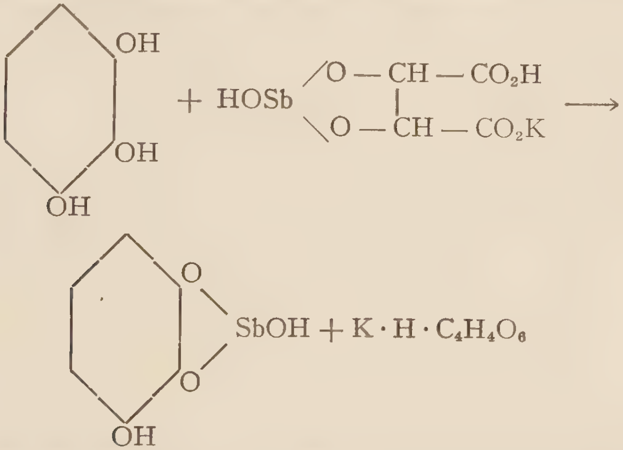
[59] Mackey: *J. Chem. Soc.*, **95** (1909), 604.
[60a] Rosing: *Compt. rend.*, **46** (1858), 1140.
[b] Causse: *Bull. soc. chim.*, [3] **8** (1892), 245.
[61] Causse: *Ann. Chim. Phys.*, [7] **14** (1898), 526.

Preparation. 1. Pyrogallol and its derivatives possess such a strong tendency to form stable antimonyl compounds that they react with potassium antimonyl tartrate in aqueous solution to form antimonyl pyrogallol or its derivatives.[60a, 61] This reaction is much more rapid in hot than in cold solutions and affords a very convenient method of preparing antimonyl compounds of this class.



During the mordanting of cloth with tannic acid and tartar emetic, antimonyl tannic acid forms in a manner similar to that indicated above, but the composition of the product is variable and depends upon the conditions under which it is formed.[62] Thus, when tartar emetic is in excess, the products formed in cold and hot solutions are represented by the empirical formulæ $C_{14}H_9(SbO)O_9$ and $[C_{14}H_8(SbO)O_9]_2SbOH$ respectively. In dilute solutions in the absence of excess tartar emetic the composition of the product is represented by $(C_{14}H_9O_9)_2SbOH$. The catechol derivatives have not as yet been prepared by this process.

2. A method of preparation which does not utilize the difference between the affinities of aromatic and aliphatic hydroxyl compounds for the antimonyl group involves the use of antimony trichloride and is applicable to di- as well as tri-hydric phenols. In the cases of water soluble phenols, the reaction with antimony trichloride may be carried out in aqueous hydrochloric acid or sodium chloride solutions;[63] the electrolytes are used to prevent hydrolysis

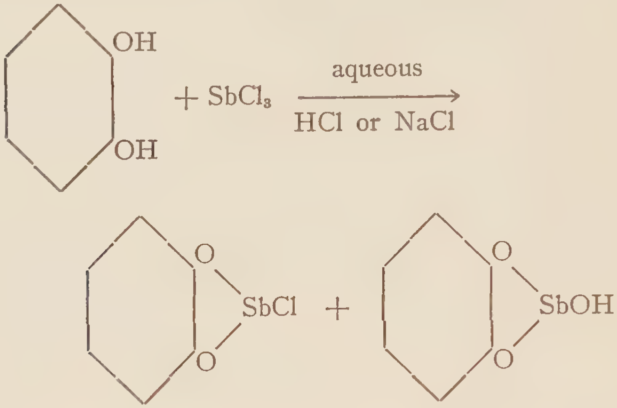
[62] Sanin: *Amer. Chem. Soc. Abst.*, 4 (1910), 1296.

[63a] Ref. 60b.

[b] Causse: *Compt. rend.*, 115 (1892), 507; 125 (1897), 954.

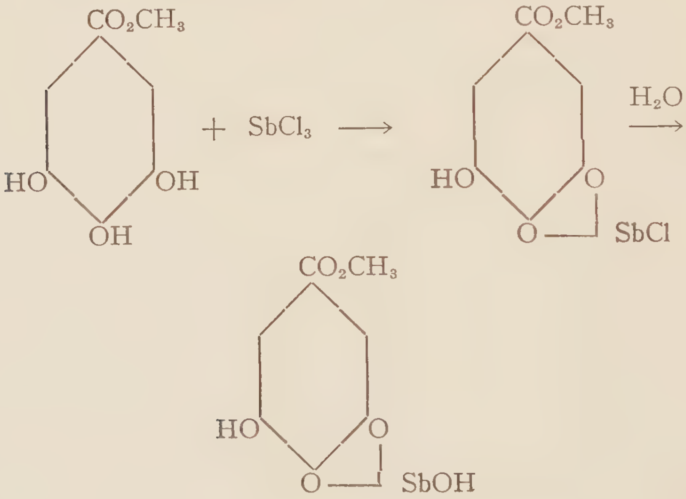
[c] Ref. 61.

of the chloride before reaction occurs. In acid solution the product is the chloride of the antimonyl compound contaminated with a small amount of the hydrolysis product; in salt solution, however, the reverse is true and the chloride is the contaminant.



The reaction mixture may be converted completely into the hydroxide by boiling with water or into the chloride by treating with concentrated hydrochloric acid.

In a modification of this process, alcohol is used as a reaction medium instead of aqueous acid or salt solutions.[64]



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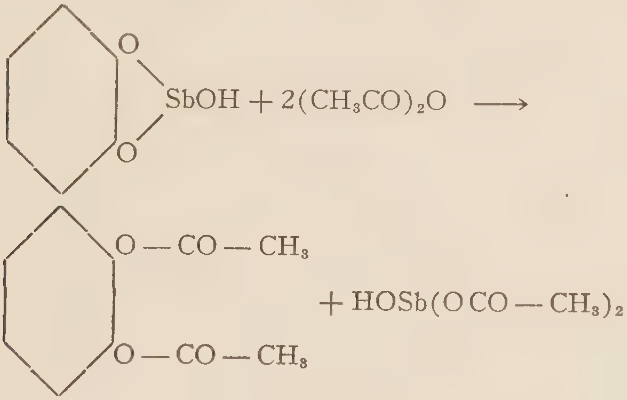
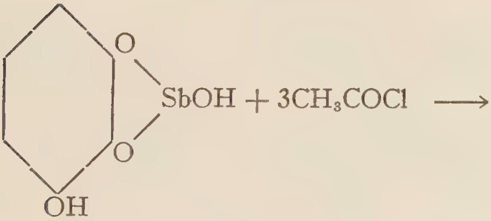
[64] Ref. 61, p. 557.

Properties. The antimonyl derivatives of polyphenols are colorless solids which are insoluble in water or neutral solvents but soluble in acids or alkali hydroxides. The antimonyl group is bound quite firmly as compared with the analogous aliphatic antimonyl compounds or the trialkyl or aryl esters of antimonious acid. Hydrolysis does not occur even in warm acid or alkaline solution, but when these substances are heated in a sealed tube with acetic anhydride[65] or acetyl chloride,[66] decomposition occurs.



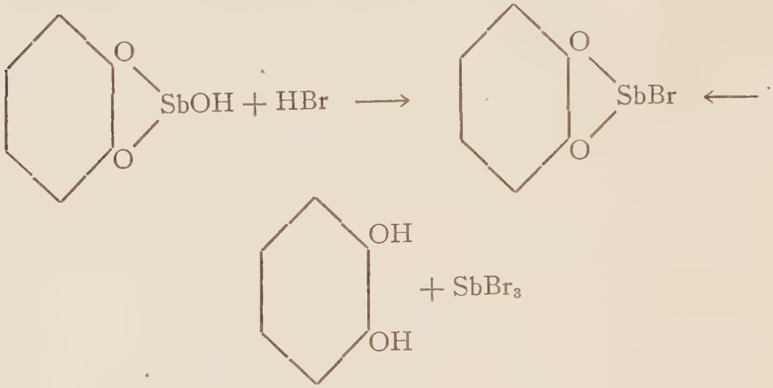


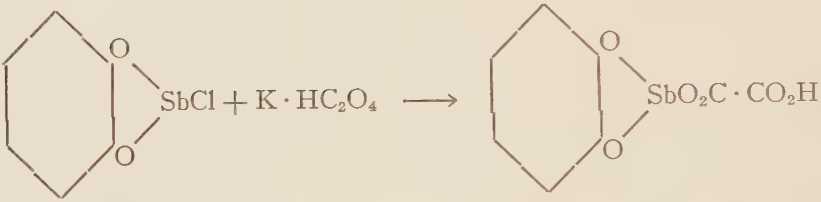
$$1,2,3 - C_6H_3(O - CO - CH_3)_3 + SbCl_3 + H_2O$$

The hydroxyl group which is attached to the antimony atom may be replaced by other negative groups or atoms; upon warming with concentrated hydrochloric or hydrobromic acids the corresponding halides are formed. The bromides may also be obtained by the action of antimony tribromide on the polyphenol; substitution of the tri-iodide and fluoride for antimony tribromide in this method is the best way to obtain the iodine and fluorine derivatives of the antimonyl compound.[67, 68] The acetate may be secured from a

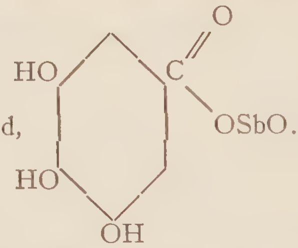
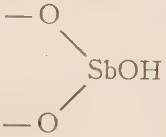
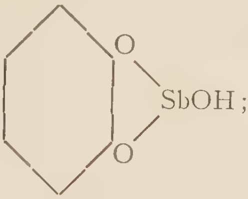
[65] Causse: *Bull. Soc. Chem.*, [3] **8** (1892), 245.
[66] Causse: *Compt. rend.*, **115** (1892), 507.
[67] Causse: *Ann. Chim. Phys.*, [7] **14** (1898), 526.
[68] Causse: *Compt. rend.*, **125** (1897), 954.

glacial acetic acid solution of the antimonyl phenol; potassium acid oxalate converts the chloride into the oxalate.[67]





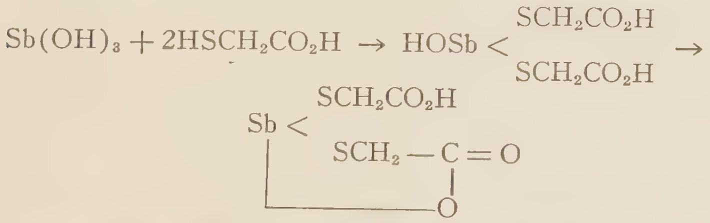
Although the antimonyl derivatives of this type are quite stable, hydrogen sulfide precipitates the antimony as the trisulfide in acid solution.

Structure. Berzelius obtained an antimonyl derivative of gallic acid by treatment with tartar emetic and considered his product to be a salt of gallic acid,  However, this substance may be converted into a crystalline potassium salt by the action of potassium bicarbonate,[67] and antimonyl derivatives can be secured from methyl gallate and from polyphenols in which carboxyl groups are absent but not from benzoic acids in which hydroxyl groups are not present. Therefore, in these substances the antimonyl group is united to hydroxyl groups rather than the carboxyl group. Inasmuch as stable products can be obtained only from ortho phenols, it is probable that the group  is present, e.g.,  analytical data also agree with this type of formula.

D. Antimonyl Thioglycollates.

Antimonials analogous to the aliphatic compounds containing a Sb-O-C linkage have been prepared in which the oxygen atom is replaced by sulfur and found to be chemically very similar to the oxygen compounds. As yet studies in this field have been limited to antimonials prepared from thioglycollic acid and its derivatives.

Preparation. 1. Thioglycollic acid and its ethyl ester react with antimony oxide in much the same manner that hydroxy acids do; the hydrogen of the — SH group is replaced by antimony. In the case of the free acid, the reaction is carried out by boiling an aqueous solution of it with antimony oxide;[69] the latter, therefore, probably reacts in its hydrated form.



$$Sb(OH)_3 + 2HSCH_2CO_2H \rightarrow HOSb{<}\begin{matrix}SCH_2CO_2H\\SCH_2CO_2H\end{matrix} \rightarrow$$

This substance was first prepared by Rosenheim and Davidsohn,[70] but the formula ascribed to it, $Sb(SCH_2CO_2H)_3$. was in-

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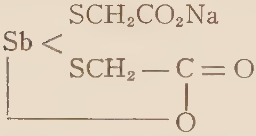
[69a] Klason and Carlson: *Ber.,* 39 (1906), 732.
[b] Ramberg: *Ibid.,* p. 1356.
[70] Rosenheim and Davidsohn: *Zeit. anorg. Chem.,* 41 (1904), 246.

correct; the error was subsequently admitted.[71] However, when the ester is employed, the reactants are mixed in the absence of any solvent.[72]

$$Sb_2O_3 + 6HSCH_2CO_2C_2H_5 \rightarrow 2Sb(SCH_2CO_2C_2H_5)_3 + 3H_2O$$

2. An alternative method by which antimony thioglycollic acid may be prepared involves the use of antimony trichloride dissolved in dilute hydrochloric acid.[73]

Properties. Antimony thioglycollic acid is a white crystalline substance which is insoluble in water, but soluble in hydrochloric acid. By the addition of the calculated quantity of sodium, potassium, or barium carbonates, the corresponding salts are obtained, which, with the exception of the potassium salt, are crystalline.[74] Sodium antimony thioglycollate is represented by the formula



; an excess of alkali decomposes the internal salt. Alcoholic caustic potash decomposes the compound with the formation of potassium antimonite.

Ethyl antimony thioglycollate is an oil which has very little tendency to crystallize; in alcoholic solution it reacts readily with ammonia to form antimony thioglycollamide[75] $Sb(SCH_2CONH_2)_3$, which is also an oil which crystallizes slowly. Caustic alkalies decompose the amide in aqueous solution with the precipitation of antimony trioxide; aqueous solutions of the amide gradually deposit a small quantity of antimony trisulfide.

The stability of the sulfur compounds appears to be intermediate between that of the aliphatic antimonyl compounds and that of the antimonyl derivatives of the polyphenols.

[71] Rosenheim: *Zeit. anorg. Chem.*, 57 (1908), 359.
[72a] Rowntree and Abel: *J. Pharm. and Exper. Therap.*, 2 (1910), 109.
[b] Brunner: *Arch. Exper. Path. and Pharm.*, 68 (1912), 193.
[73] Klason and Carlson: *Ber.*, 39 (1906), 732.
[74] Ramberg: *Ibid.*, p. 1356.
[75] Ref. 72a, p. 110.

Chapter 6.

Antimonials as Therapeutic Agents.

By

GEORGE C. SHATTUCK, M.D.

A. Types of Disease in Which Antimonials are of Special Value.

Antimonials administered by mouth had formerly a great vogue but their use in ordinary medical practice later declined until they had become practically obsolete as therapeutic agents. Within recent years, however, they have been found to have great value in the treatment of certain diseases of the tropics.

The chemical relationship of antimony to arsenic led Nicolle in 1906 to suspect that derivatives of antimony might have therapeutic value similar to that of arsenicals in the treatment of African sleeping sickness. This disease bears no relation to what is now called "sleeping sickness" in the United States. The term was originally applied to an African malady which has been called trypanosomiasis since the discovery of the protozoan organism of the genus Trypanosoma which causes the disease.

The Trypanosomes. Trypanosomes may be found as parasites in the blood of all classes of vertebrates including reptiles, fish, birds and mammals. Some kinds are actively pathogenic for their hosts, whereas others seem to be nearly innocuous. The several species found in man are not only pathogenic for man but also for certain other mammals, such as the experimental animals of the laboratory. Most of the species of trypanosomes commonly found in animals seem, as a rule, to be innocuous to man, but some of them so closely resemble those of man as to render classification difficult and differentiation uncertain.

Although species differ somewhat in form and in size, the trypanosomes are characterized by a sinuous body tapered at the ends, an undulating membrane disposed longitudinally, and generally by a single, long flagellum projecting anteriorly. The length of the body is several times the diameter of a red blood corpuscle. Trypanosomes are actively motile, swim freely about in the blood, and may escape from the blood vessels into the intracellular spaces of any organ of the body. They are most easily found in the blood during paroxysms of fever, when they may be extremely numerous. but in the intervals between paroxysms it may be impossible to find any at all by microscopic examination of the blood, the gland juice, or the cerebro-spinal fluid. It is sometimes possible to demonstrate the presence of trypanosomes in the blood by means of cultures when they cannot be detected there by other means.

African trypanosomiasis of man is caused by T. gambiense, by T. rhodesiense (which some persons believe to be the same as T. brucei mentioned below), or by T. nigeriense which produces a milder form of disease. The early symptoms in man are irregular fever, enlargement of the lymph glands, local edema of the skin, and sometimes erythema. Later, the spleen and sometimes the liver becomes enlarged, and, in the final stage, there is somnolence and other evidence of involvement of the central nervous system. Hence the name of sleeping sickness. When the disease has reached this stage spontaneous recovery is not to be expected and treatment is practically hopeless.

South American trypanosomiasis of man, or Chagas's disease, which is caused by T. cruzi, has a very different clinical picture, but inasmuch as this disease has thus far proved refractory to antimonials and to all other drugs tried, it may be passed over here without further comment.

The important trypanosomiases of domestic animals are nagana, surra, "mal de caderas," and dourine. These diseases are caused respectively by T. brucei, T. evansi, T. equinum, and T. equiperdum. They have great economic importance because all of them are fatal to horses, and surra attacks cattle, camels, and domestic buffaloes as well. Nagana is particularly prevalent in South Africa, surra in Southern Asia, Malay and the Philippines, and "mal de caderas" in South America. Dourine is found in Southern Europe, North Africa, and Chile. It may, perhaps, exist in the United States.

The natural mode of transmission of most forms of trypanosomiasis is through the medium of biting insects. In Africa certain species of Glossina, commonly known as "tse-tse flies," are particularly implicated. Dourine, however, is transmitted by sexual contact.

Much experimental work on the use of drugs for the treatment of trypanosomiasis has been performed with rats or mice infected artificially. The parasites of nagana and of surra have been most commonly used. They cause fatal diseases in these rodents. T. lewisi is common in rats the world over but is practically harmless to them. For experimental purposes trypanosomiasis is transmitted by inoculation of infected blood from a diseased into a healthy animal. Rats, mice, guinea pigs, dogs, rabbits, monkeys and larger domestic animals have also been used for the study of trypanosomiasis, and extensive tests of the value of arsenicals and antimonials have been made upon man.

The Leishmanioses. Under this head will be described several allied diseases which can be treated successfully with antimonials but for which arsenicals are practically valueless. This group of diseases is caused by protozoan parasites of the genus Leishmania which is included in the family of the Trypanosomidæ.

Two species of Leishmania are recognized, namely, L. donovani and L. tropica. Although apparently identical morphologically and culturally, they produce very different lesions in man. L. donovani causes a general infection called kala-azar which is characterized by fever, enlargement of liver and spleen and serious systemic disorders. This disease is common in India and China, and, unless adequately treated, it is almost invariably fatal. L. tropica, on the other hand, as far as is known, causes only local lesions which may affect the skin and subcutaneous tissues or the mucous membranes of the nose and throat. The mildest form of disease caused by L. tropica is particularly associated with the Near East, where it is called "Oriental sore" or "Bagdad boil." It may heal spontaneously, but only after many months. In South America very disfiguring lesions of a destructive and chronic character are caused by L. tropica in or about the nose and mouth. This condition is called "uta" or "espundia." Chronic ulcerative lesions, when they appear on other parts of the body, are called "forest yaws."

Organisms are found abundantly in the liver and spleen in kala-azar, and they may even be demonstrable in the blood in this disease. In the lesions of Oriental sore Leishmania is numerous, but in the South American chronic forms of leishmaniosis the organism is scarce and difficult to find. The Leishmania is much smaller in diameter than a red blood-corpuscle. As seen in the tissues, it is round or ovoid in shape, and many organisms may be found lying between cells or enclosed within large phagocytes. Developing forms, thus far found only in cultures, are pear-shaped or elongated and present a single flagellum at the end. Beyond this nothing is certainly known of the life history of Leishmania, but the bed-bug has been suspected of playing a part in transmitting the infection.

Kala-azar occurs naturally in dogs but they are difficult to infect artificially with Leishmania. Monkeys can sometimes be infected artificially.

The Schistosomiases. Schistosomiasis is a terrible scourge in Egypt and in parts of South Africa and of China, and it is found less commonly in many other parts of the world. The use of antimonials against the three varieties of Schistosoma which infest man has produced so satisfactory results that antimonials are regarded as specifics for these diseases. They have proved less valuable, however, in a number of disorders caused by related parasites in man and animals. Arsenicals have not proved useful against the schistosomiases.

The schistosomiases of man are caused respectively by Schistosoma hæmatobium, S. mansoni and S. japonicum. These organisms are flat worms or "flukes" which reach maturity in the branches of the portal system of the liver. From there they migrate during the period of reproduction to the venules of the urinary bladder or of the intestine where the ova are discharged near the surface of the mucous membrane. Inflammation, ulceration and hemorrhage result and the ova appear in the urine or in the fæces. Fibrosis of the liver, dropsy and splenic enlargement may result in cases of severe infestation, and secondary complications in the genito-urinary tract or in the intestine are of frequent occurrence. Many patients suffer severely for years and many deaths result. Hundreds of worms may be found in a single patient. When but few worms are present symptoms may be slight or entirely absent. The ova of S. hæmatobium are generally discharged in the urine and those of S. mansoni and of S. japonicum in the fæces. When passed into water, the ovum quickly hatches, liberating a miracidium which swims about freely until it can find a fresh-water snail of a special genus. The miracidium enters the snail, undergoes a further stage of development and emerges a cercaria which, again, swims in the water. The cercaria is capable of penetrating the normal skin of man or other suitable vertebrate host. It then passes by way of the blood or lymphatic vessels to the liver, where it develops into the adult form.

Antimonials have been used with complete success in many thousand cases of disease caused by S. hæmatobium, and in numerous cases due to S. mansoni. As yet they have not been used extensively against S. japonicum, but cases treated successfully have been reported.

The use of tartar emetic in sufficient dosage causes the ova of the schistosome to shrivel and to turn black. They are then incapable of hatching. Further use of the drug kills the adult worms, but sterile ova may continue to be discharged for some time from the mucous membranes in which they had been deposited before the death of the worms.

Monkeys, mice, and rats are susceptible to infection with S. hæmatobium.

Granuloma Inguinale. Inguinal granuloma is a very chronic, granulomatous process developing in the skin and subcutaneous tissues and leading to ulceration. The disease, so far as known, does not heal spontaneously and the lesion generally spreads very gradually. Almost invariably it attacks the genitalia or neighboring parts. The neighboring glands are not involved unless by secondary or coincident infection of another kind. Syphilis is frequently coexistent in the same individual. The causative organism of inguinal granuloma is not certainly known and it is doubtful whether it has been cultivated.[1] The disease is believed to be transmitted, ordinarily, by direct contact during sexual relations.

Treatment by means of antimonials usually gives excellent results but some cases have failed to respond to the drug. Other methods of treatment are rarely successful. Arsenicals are useless except for coincident syphilis.

Leprosy. Articles recently published indicate that antimonials may prove to have an important place in the treatment of the ulcerative lesions of leprosy. Arsenicals have little, if any, value for leprosy.

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[1] Donovan first described peculiar bodies seen in large phagocytic cells. Later observations make it appear that the bodies seen by Donovan are masses of bacilli similar in appearance to Bacillus mucosus capsulatus of Friedländer, and very like the bacillus of rhinoscleroma. Histological changes, too, of inguinal granuloma are very like those of rhinoscleroma. It seems probable that inguinal granuloma is caused by a bacillus as above described. Although not easily recognized except when grouped within a phagocytic cell, it is thought that the bacilli may lie also between cells.

B. Action of Antimonials in the Body.

Pathology. After fatal poisoning from antimonials in man one finds intense congestion of the alimentary canal with hemorrhages into the mucous membrane, and cloudy swelling and fatty degeneration of such organs as the liver, kidneys, and heart.[2]

Distribution of the Drug. Brunner[3] administered tartar emetic to dogs by mouth and subsequently recovered considerable quantities of it from the livers and spleens. Traces of antimony were found in the brain. Ciechanowski,[4] experimenting similarly with rabbits, obtained relatively more antimony from the kidneys than from the liver, and showed that, after prolonged administration of the drug, the amount in the liver increases. He found antimony in the heart, lungs, and muscles as well.

Toxicity in Man. Acute poisoning in man causes death by prostration with paralysis of the respiratory center and of the heart. Toxic doses of the drug tend to cause a marked fall of blood pressure, rapid action of the heart, vomiting and diarrhœa. In mild cases of poisoning the flow of urine is increased but in more severe cases it becomes scanty and contains blood. The secretion of urine may even be suppressed.

When antimonials are used therapeutically in man the early signs of poisoning to be watched for particularly are stiffness and pain in the muscles about the shoulders, loss of appetite, nausea or vomiting, loss of weight, albuminuria, and rapidity of the heart. Skin eruptions are seen occasionally. These signs call for interruption of the treatment and reduction of dosage.

Immediately after an intravenous injection of an antimonial, patients frequently experience a sense of constriction in the chest which is often associated with irritation in the throat and spasmodic cough. There may be transient dizziness or syncope, nausea or vomiting. These symptoms are more common after the first few doses than subsequently. When such symptoms are slight, treatment may be continued cautiously. When a case of trypanosomiasis or of kala-azar in which parasites are numerous receives an effective dose of an antimonial intravenously, a febrile reaction may occur. Such reactions have been attributed to the products of rapid destruction of the parasites. On the other hand, febrile reactions following the injection of antimonials, apparently, may be due at times to other causes.

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[2] Stevens: "Textbook of Therapeutics," 6th ed., 1923, p. 283.

[3] Brunner: *Arch. f. exp. Path. u. Pharm.*, **68** (1912), 186.

[4] Ciechanowski: *Ann. d'Hyg. Pub.*, [3] **40** (1898), 125.

Ordinary dosage cannot safely be used for patients who are enfeebled or who have severe lesions of the kidneys, liver, heart or lungs. After repeated injections of an antimonial, cumulative toxic effects may develop. A number of deaths have been reported from the therapeutic use of antimonials but, with the knowledge now available, such accidents should be very rare in future.

Because of their pronounced irritating effect upon the stomach, antimonials have been little used by mouth in recent years but large daily doses of tartar emetic well diluted with water have been successfully administered by mouth and also by rectum. The former tend to cause nausea and the latter seems to irritate the lower bowel.

Various antimonials have been recommended for subcutaneous or for intramuscular injection, but they have not been very widely used in either of these ways because of the local irritation generally produced. Some of these compounds are far more irritating than others. Plimmer and Thomsen,[5] when injected sodium antimonyl tartrate into rats, observed no evidence of pain or inflammation at the point of injection in the rat but, in man, on the contrary, this compound has proved so irritating that its use, except by the intravenous route, has been abandoned.

The intravenous route is commonly preferred for antimonials in the treatment of human disease but, even so, ill effects cannot always be avoided. Thrombosis of the vein at the point of injection, painful inflammation around the vein from leakage of the solution into surrounding tissues, or abscess formation may result from the injections.

Toxicity in Animals. In experiments with guinea pigs and white rats after injections of toxic doses of an antimonial, Brahmachari[6] found hemorrhages in the lungs, destructive processes with hemorrhage in the kidney, fatty changes and cellular infiltration in the liver, destruction of the splenic pulp and abnormalities in the pituitary body and in the parotid glands.

After a single intramuscular injection of an antimonyl tartrate or malate into guinea pigs, he observed, in rare instances, that death might result from delayed poisoning after three weeks or more.

[5] Plimmer and Thomsen: *Proc. Roy. Soc. of London,* [B] **80** (1908), 1.
[6] Brahmachari: *Indian Jour. of Med. Research,* **10** (1922), 492.

In such cases pathological changes were found in the lungs, liver, and kidneys, and the presence of antimony in these organs was shown by chemical tests.

Excretion. Antimonials are excreted chiefly by the stomach and bowel but partly by the kidneys, skin and respiratory tract.[7]

C. Methods of Treatment with Antimonials.

Antimonials and arsenicals have been tried for sleeping sickness by injection subcutaneously, intramuscularly, and intravenously and they have been administered by mouth and by rectum. Antimonials have also been used in ointment form by inunction and arsphenaminized serum has been injected into the spinal canal in sleeping sickness.[8] If antimonialized serum has been so used I have failed to find a reference to it.

There is no generally accepted standard method of administering antimonials for sleeping sickness or for the various other diseases for which they are used. Comparison of methods shows that a large number of different antimonyl compounds have been recommended, but that intravenous injections of antimonyl tartrates, dissolved in normal salt-solution, have been most frequently employed.

Dosage of Tartar Emetic. The initial dose of tartar emetic varies from 16 to 65 mg. (¼ to 1 grain), and increasing amounts are administered subsequently up to 130 or rarely 195 mg. (2 or 3 grains) per dose. Total dosage for a case of trypanosomiasis may exceed 5 grams (75 grains) but for kala-azar 2 grams (30 grains) may suffice and schistosomiasis or inguinal granuloma can generally be cured with from 1 to 2 grams (15 to 30 grains). The drug can be given daily in courses of from ten days to two weeks duration, the intervals between courses being from 15 to 30 days, or on alternate days for three weeks or a month, or biweekly doses can be used for a month or more. Less frequent administration seems to be ineffective.

Human trypanosomiasis may require a series of courses of treatment lasting from one to two years. For this disease arsenicals are often used in conjunction with antimonials or in alternate courses. In kala-azar a cure may be expected within two or three months, in inguinal granuloma within one month or six weeks, and in schistosomiasis, as a rule, within one month.

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[7] Stevens: "Textbook of Therapeutics," 6th ed., 1923, p. 283.

[8] Yorke: *Tropical Diseases Bulletin,* **18** (1921), 155.

Administration of Tartar Emetic. A 1% solution has often been recommended in the belief that stronger solutions are more likely to damage the vein, but solutions of 0.1% have been preferred on the same ground.[9] On the other hand, Baujean[10] and others have used 2% solutions in the belief that when a small quantity of menstruum is used, general reactions from the drug are less severe and Borja and Amaral[11] even recommended a 4% solution.

In order to minimize distressing immediate effects, the solution should be slightly warm when administered and the injection should be given very slowly. A 10 cc. glass syringe is often used for the injections but many clinicians prefer to administer the remedy with funnel and tube. They inject a little salt-solution before and after the solution of the drug as a precaution against getting any of it into the tissues.

Preparation of Tartar Emetic. Methods of preparing potassium antimonyl tartrate for injection differ widely. There are many physicians who believe that solutions of this drug may deteriorate rapidly on keeping.[12] To prevent this they have single doses of the powdered drug put up in papers or tablets. They then dissolve the required dose at the bedside, boil the solution, and inject it while still warm.

Other physicians recommend sterilization of the solution by the fractional method or by Berkfeld filtration because they think that the high temperatures of the autoclave may cause the drug either to lose potency or to become more toxic. Borja and Amaral[11] sterilized the powdered drug with chloroform and subsequently dissolved it in sterile salt-solution. This is a convenient method for use in the field. Still other physicians see no objection to autoclaving the drug. They prepare a strong solution of the drug in distilled water, sterilize it in the autoclave, put it up in small bottles like a vaccine, and keep it on hand for indefinite periods. Such solutions are autoclaved again before use, and are generally diluted with salt-solution to the required strength before being injected. Another method is to prepare a stock solution of suitable strength for injection in normal saline, to sterilize it in the autoclave, and to keep it indefinitely in flasks. Stock solutions of potassium antimonyl tartrate must be made from a pure product, must be sterilized,

[9] McDonagh: *Jour. Trop. Med. and Hyg.*, 23 (1920), 165.
[10] Baujean: *Bull. Soc. de Path. Exot.*, 14 (1921), 299.
[11] Borja and Amaral: *Arch. Brasil. de Med. & Chir.*, 5 (1915), 145.
[12] Brahmachari: *Indian Jour. Med. Research*, 11 (1923), 196.

and must be protected from contamination because fungi may, otherwise, grow in them.

Other Antimonials. Various organic compounds of antimony have been highly recommended for kala-azar and a number of "colloidal" preparations of the metal or of the sulfide have given encouraging results. Preparations of both kinds have been used intravenously but the sulfide has been recommended particularly for intramuscular injection. Metallic antimony and some chloride compounds have been used successfully by inunction for experimental infections in small animals. Certain preparations of antimony-oxide have been recommended for use intramuscularly and a number of antimony compounds, including antiluetin,[13] have been tried intramuscularly, intravenously, and by mouth.

Advantages of Antimonials. The great importance of antimonials in the treatment of human disease is that they have a curative effect in the dangerous and distressing diseases above mentioned. In the treatment of these diseases, except trypanosomiasis, they have no rival and their action is well-nigh specific. Moreover, it has been shown experimentally that some of the antimonyl tartrates will protect animals from trypanosome infection for a short period after the injection, although not for any great length of time. This fact has been put to practical use when cattle were to be driven across an area infested with tse-tse flies where animal trypanosomiasis was rife. Again, antimonials may be effective in cases of sleeping sickness resistant to arsenicals, e.g., in the form of the disease caused by T. rhodesiense, or against races of trypanosomes which have acquired tolerance to arsenicals.

Antimonials Compared with Arsenicals. Arsenicals are effective in syphilis and in various other spirochætal diseases such as relapsing fever, diseases for which antimonials are not used. On the other hand, antimonials are preëminent in the treatment of the group of diseases above described with the exception of trypanosomiasis. In the treatment of this disease the two drugs seem to be of approximately equal value but neither of them can be relied upon for prompt cure of African trypanosomiasis in man, even when treatment is begun early in the course of the disease. In the later stages treatment nearly always fails.[14]

[13] A double salt of potassium and ammonium antimonyl tartrates. Tsuzuk: *Deut. med. Wochschr.*, 39 (1913), 985.

[14] "Baeyer 205" is probably superior to any of the arsenicals or antimonials with respect to trypanosomiasis.

Atoxyl has a marked advantage over potassium antimonyl tartrate in that it is satisfactory for intramuscular injection. It is used in 10% solution in normal saline. The powdered drug keeps well and dissolves readily, but the solution should be freshly prepared because it is unstable. The usual dosage is from 195 mg. (3 grains) to 455 mg. (7 grains). The smaller dose may be administered every third day or the larger dose every fifth day. If signs of arsenical poisoning develop, the treatment is suspended. The most serious disadvantage of atoxyl and of some of the newer arsenicals which have been used in the treatment of trypanosomiasis is that cases of optic atrophy with permanent blindness have resulted from its use in large dosage. Visual disturbances, at least of a transitory character, have been caused by some of the newer arsenicals. The older arsenicals do not affect the eyes but are of comparatively little value in sleeping sickness. Antimonials do not cause optic atrophy. Arsenicals and antimonials are similar in their tendency to produce gastro-intestinal irritation, dermatitis and neuritis.

D. Therapeutic and Experimental Observations.

Therapeutic limitations. The use of arsenicals and of antimonials is limited, firstly, by the fact that therapeutic dosage overlaps toxic dosage and that excessive dosage may involve serious consequences including death of the patient. Therefore, patients under treatment require careful medical supervision.

Secondly, the use of these drugs is restricted by the technic required for their employment. They should be administered only by a physician skilled in this kind of therapy or, at least, under the supervision of such a physician.

Thirdly, in African sleeping sickness of man a cure can only be expected in the earlier stages of the disease, and then only after a very long course of treatment. In South American trypanosomiasis no known treatment is effective.

Natural Resistance of Trypanosomes. It is well known that infections in man do not always respond in the same way to treatment as do infections with the same organism in an animal, and, further, it is known that the *same species* of trypanosome infecting different species of mammals may be more resistant to treatment with *the same drug* in one species than in another species.[15] The

[15] Nicolle and Mesnil: *Ann. de l'Inst. Past.*, 20 (1906), 417.

experimental worker must remember, too, that different kinds of mammals differ in their ability to tolerate poisonous drugs; and that *different species* of trypanosomes are, by nature, more or less resistant to medication. For example, arsenicals seem to be of less value in sleeping sickness due to T. rhodesiense than are antimonials, but the milder form of disease caused by T. nigeriense may be expected to yield to atoxyl. Strains or races of the same species of trypanosome emanating from different localities may show marked differences in virulence as well as in amenability to treatment. Virulence and resistance to drugs, however, may bear no relation to each other. The virulence of a strain long maintained under laboratory conditions may diminish or even disappear.

Resistance of the Host to Disease. The course of disease due to a trypanosome infection is influenced to an important degree by the natural resistance of the host to the infection. According to Taliaferro and Taliaferro [16] this resistance may act in either of two ways or in both ways: namely, by retarding reproduction of the trypanosomes or by destroying them. They describe a method of measuring resistance of the host.

It has been repeatedly observed in animals that when a trypanocidal drug is administered in excessively toxic dosage the disease may progress without interruption. The usual explanation is that the poisonous effects of the drug have destroyed the natural resistance of the host to the infectious process.

Tolerance of Trypanosomes. It has been shown by animal experimentation [17] that when repeated doses of an arsenical are injected into an animal in amounts which fail to kill all of the trypanosomes, the latter may acquire tolerance ("resistance" or "fastness") to arsenicals. A race of trypanosomes thus rendered tolerant manifests this tolerance for all arsenicals of the same chemical group (Ehrlich), but it may yield to arsenicals of another group, or to antimonials. Similar tolerance has been developed for antimonials [17] but generally, if not always, by strains already tolerant to arsenicals.

Tolerance to a drug may be lost by a strain of trypanosomes when transferred by inoculation to another animal of the same species. On the other hand, tolerant strains may sometimes retain this quality through many transfers and for periods of many months.[17] Transfer to an animal of a different species generally, if not always, destroys tolerance, and tolerance to atoxyl in man has been observed to disappear after a course of treatment with an antimonial. Observations relating to tolerance developed by trypanosomes for antimonials appear to be discordant even in animal experiments, but tolerance to atoxyl seems to develop with considerable regularity in experimental trypanosomiasis. Little is known about tolerance in human trypanosomiasis but it seems probable that if, in a case of sleeping sickness in man, the trypanosomes should become tolerant to arsenicals of one group, the patient might still be cured with an arsenical of another group or with an antimonial. The degree of tolerance to antimony of a race or strain of trypanosomes can be tested satisfactorily in vitro. Tests of this kind can be used with some of the arsenicals but not with atoxyl.[17]

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[16] Taliaferro and Taliaferro: *Amer. Jour. of Hyg.*, 1922, II, p. 264.

[17] Mesnil and Brimont: *Ann. de l'Inst. Past.*, 22 (1908), 856.

Tolerance of the Host. The tolerance of animals or of man himself to antimonials, it seems can not be increased materially.

Trypanocidal Activity. When a single dose of an actively trypanocidal drug is injected into an animal infested with a trypanosome which has neither natural resistance nor acquired tolerance to that drug, the trypanosomes disappear entirely from the blood-stream and from the lymphatic glands within a few minutes or hours. Observation has shown that the parasites in the blood cease to move, become swollen, and disintegrate. The blood then remains free from parasites, as a rule, for a number of days, and the animal may seem quite well. If, however, as is generally the case, some trypanosomes have remained alive somewhere in the animal, a relapse will take place and numerous parasites may again be found in the blood. If the drug be readministered once during each relapse in dosage insufficient to kill all the trypanosomes the relapses may recur at shorter and shorter intervals, and, finally, the drug may be without effect as the result of the development of tolerance for it by the parasites.

Studies of the trypanocidal action of antimonials by Voegtlin and Smith[18] indicate that there is a sharply defined threshold (minimum effective dose) below which the drug fails to affect the parasites. This threshold, they say, is due in part to the nature of the reaction between the drug and the parasites and in part to absorption of the drug by the tissues of the host. The process curve

[18] Voegtlin and Smith: *Jour. of Pharm. & Exp. Therap.*, **15** (1920), 453.

is orderly and consistent throughout individual experiments but various experiments indicate two general types of reaction, differing in velocity. In one type the reaction velocity remains constant, whereas in the other type the velocity increases constantly. They describe and recommend a method for rapid and accurate determination of the trypanocidal power of drugs.

Comparative Therapeutic Dosage. Therapeutic success depends to a great extent on the ability of the man or animal to tolerate effective dosage.[19] In general, small animals can withstand very much larger dosage of antimonials in proportion to body-weight than can man or the larger animals. Small animals, consequently, are easier to cure. Moore[20] has advanced the opinion that heavy metals chiefly damage the intestinal mucosa in the process of excretion, and that dosage for them should be calculated on the basis of body-surface which increases as the ⅔ power of body-weight.

E. Requirements for a Drug as a Satisfactory Therapeutic Agent.

Requirements for a drug which can be considered a satisfactory therapeutic agent may be discussed under several heads.

First: the effective therapeutic dose should be far below the toxic dose. This is important because errors of preparation or administration occasionally result in the use of ten times the dose intended, and because a patient in taking a drug which has been prescribed for him sometimes acts on the principle that if some is good, more is better. It is a common experience, too, that some individuals have what is called an idiosyncrasy to certain drugs, i.e. such a person cannot take a certain drug or any drug of a certain group in ordinary dosage without being more or less severely poisoned thereby. No way is known of anticipating idiosyncrasies to drugs in individuals. Low toxicity is particularly desirable for drugs which are to be put into the hands of patients.

Second: ease of administration is extremely advantageous. A drug which can be used safely and effectively in pill or tablet form by mouth, or which can be prescribed in solution, demands fewer visits to the physician and has, therefore, a much wider application than a drug which can be administered only by a person trained in the technic of its use. Dangerous drugs not only must be administered by the physician, but may necessitate keeping the patient in hospital under close observation; and hospital treatment is expensive.

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[19] Sergent, Donatien and Lheritier: *Ann. de l'Inst. Past.*, **35** (1921), 207.
[20] Moore: *Bio-Chem. Jour.*, **4** (1909), 323.

Third: stability, in spite of extremes of heat, dampness or cold incidental to climate, is a quality of great value because a drug which decomposes readily entails financial loss in any case and it may either lose potency or acquire toxicity. It is advantageous to have a drug which can be kept ready for use for long periods and can be dispensed in powder, tablet, pill or solution according to its nature.

Fourth: a drug which is to be used in the treatment of an acute disease which causes much suffering or puts life in imminent danger should be capable of affording prompt relief. Relief may be imperatively required within a few minutes, hours, or days according to the nature of the malady. In less urgent conditions it is essential that relief should be sufficiently prompt and definite to encourage the patient to continue the treatment until cured.

Fifth: a drug to be administered by mouth need not be readily soluble in water but it should be capable of complete and sufficiently rapid absorption by the gastro-intestinal tract under all conditions under which it may be prescribed. Drugs for use by mouth should not injure the teeth, irritate the gastro-intestinal tract or interfere with digestion.

Sixth: drugs for use by injection should be readily soluble, should withstand sterilization, should not cause pain or local irritation, and should be absorbable with sufficient rapidity to accomplish their purpose. Drugs which are moderately irritating or absorbable with difficulty are injected intramuscularly instead ot subcutaneously. When absorption is too slow, a drug may not attain sufficient concentration in the body fluids to become effective. Moreover, there is danger that it may cause cumulative toxic effects after repeated injections.

Seventh: drugs such as tartar emetic are usable intravenously although too irritating for intramuscular injection, but local irritation of the wall of the vein at the point of injection may cause thrombosis of the vein and render further injections difficult or impossible.

A satisfactory drug for intravenous use will not damage the vein or surrounding tissues even if it should leak into them. It should be soluble in a small quantity of water or normal saline, and, when injected in isotonic solution, it should not cause the blood to coagulate or to hemolyze. The solution as prepared for use should be reasonably stable and should withstand sterilization in the autoclave.

Eighth: a drug which might otherwise prove satisfactory may, perhaps, be excreted or destroyed in the body before it has had time to act upon the infecting agent. On the other hand, certain drugs which are excreted slowly tend to accumulate in the internal organs and may produce delayed symptoms of poisoning when administered repeatedly.

Ninth: tolerance to the drug should not be readily developed by the parasite against which the drug is to be used.

PART II

Chapter 7.

Organic Compounds Containing Trivalent Antimony.

A. Stibines.

Examples of the Preparation of Stibines: *Grignard reaction.*

(a) Trimethylstibine. A cold, ethereal solution of methylmagnesium iodide, prepared from 6.1 g. of magnesium, 35.5 g. of methyl iodide, and 200-300 cc. of absolute ether, is treated dropwise with an ethereal solution (80-100 cc.) of 18.9 g. of antimony trichloride; the reaction is very energetic. The flask is placed in an oil bath, and the contents of the flask are distilled in a current of carbon dioxide until the temperature of the oil bath reaches 170°. The distillate is an ether solution of trimethylstibine from which the latter is isolated as the dibromide which separates readily in white crystals when bromide is added;[1] the free stibine, which is extremely unstable in the air, may be obtained from the dibromide whenever it is to be used. Yield: 60-70%.

(b) Cyclotetramethylene-phenylstibine. A cold, ethereal solution of the magnesium compound obtained from 50 g. of 1,4 dibromobutane in 200 cc. of absolute ether is treated gradually with a solution of 40 g. of phenylstibinous chloride in 3 volumes of absolute ether with agitation. The solution is boiled for a short while and then poured into water. The ethereal layer is separated, dried with calcium chloride and evaporated; the residual oil is fractionated *in vacuo.* Yield: 15 g.; b.p. 156-158° at 20-22 mm. The entire process must be carried out in the presence of carbon dioxide.[2]

(c) Triphenylstibine. (1) An ethereal solution of phenylmagnesium bromide prepared from 20 g. of bromobenzene and 3 g.

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[1] Hibbert: *Ber.,* 39 (1906), 160.

[2] Grüttner and Wiernik: *Ber.,* 48 (1915), 1484.

of magnesium, is treated with 9 g. of antimony trichloride and refluxed for 1.5 hours. After cooling, the reaction mixture is treated with water, and the ether layer, when evaporated in a desiccator, yields colorless crystals of triphenylstibine.[3] Yield: 5.5 g.

(2) An ether solution of phenylmagnesium bromide prepared from 50 g. of bromobenzene and 7.2 g. of powdered magnesium in dry ether is treated with a 10% benzene solution containing 18 g. of antimony trichloride. After refluxing for 6 hours, the mixture is distilled with steam, and the residue is freed from diphenyl by extraction with small quantities of cold alcohol. The residual triphenylstibine is crystallized from hot alcohol.[4] Yield: practically quantitative.

Fittig or Sodium Process. Triphenylstibine. Pure, distilled antimony trichloride (40 g.) and 40 g. of chlorobenzene or 60 g. of bromobenzene are dissolved in 4 volumes of anhydrous benzene, and 50 g. of finely cut sodium is added. A reflux condenser is attached, and the flask is cooled with water in order to control the reaction. After 24 hours, the reaction mixture is warmed for a short time and filtered while hot; the insoluble matter is washed several times with hot benzene. The oil which is obtained by evaporation of the combined filtrates solidifies readily.

The crude triphenylstibine contains triphenylstibinic chloride and diphenylstibinic chloride. The latter is removed by extracting the crude material on a water bath with alcohol and some fuming hydrochloric acid. The residue is treated with petroleum ether (most of the material dissolves), and without filtering the mixture, chlorine is introduced until triphenylstibinic chloride no longer separates. The solid is collected, washed with petroleum ether and recrystallized twice from alcohol. The pure stibinic chloride is dissolved in alcoholic ammonia and treated with hydrogen sulfide; the triphenylstibine which separates is filtered out and washed with water. A second crop may be obtained by concentration of the alcoholic mother liquor. The product is recrystallized from alcohol and ether.[5]

Most of the stibines which have been prepared in this way have not been purified by such an extensive method as that used for triphenylstibine.

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[3] Pfeiffer: *Ber.*, 37 (1904), 4621.
[4] Morgan and Micklethwait: *J. Chem. Soc.*, 99 (1911), 2290.
[5] Michaelis and Reese: *Ann.*, 233 (1886), 42.

Treatment of a Potassium-antimony Alloy with an Alkyl Halide.

Triethylstibine. The potassium-antimony alloy is prepared by heating a mixture of 5 parts of potassium bitartrate and 4 parts of antimony in a covered crucible; the temperature is raised gradually, and the mass is finally maintained at white heat for 1 hour. After cooling in the absence of air, the alloy is added to 2-3 parts of fine sand and pulverized; the addition of sand is essential, because the powdered alloy when undiluted is spontaneously inflammable in the air.

The reaction between the alloy and ethyl iodide is very vigorous and can only be controlled when carried out on a small scale. A 100 cc. short neck flask is filled to ⅔ of its capacity with the alloy-sand mixture, and sufficient ethyl iodide is added to thoroughly moisten the mixture; the flask is then connected to a condenser. After a few minutes an exothermic reaction sets in, and the unchanged iodide distills off. When the latter has been completely expelled, the reaction flask is quickly disconnected and attached to a second condenser which discharges into a flask containing fresh sand-alloy mixture and which has been swept out with carbon dioxide. The reaction flask is gradually heated, and the temperature is raised until distillation ceases. The product is distilled out of the second flask in an atmosphere of carbon dioxide and collected in an apparatus which has been filled with carbon dioxide.[6]

Trimethylstibine: $(CH_3)_3Sb$

(a) From methylmagnesium iodide and antimony trichloride.[7]

(b) A mixture of a powdered alloy of antimony (4 pts.) and sodium (1 pt.) with an equal volume of sand is thoroughly moistened with methyl iodide and gently warmed, the excess methyl iodide and the trimethylstibine which volatilize, are distilled into water in the presence of carbon dioxide. The two substances combine to form tetramethylstibonium iodide which dissolves in the water. The aqueous solution is separated from the excess methyl iodide and evaporated to dryness. The dry stibonium iodide is mixed with an alloy of potassium and antimony and warmed gently; the pure trimethylstibine is collected in an atmosphere of carbon dioxide.[8]

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[6] Löwig and Schweizer: *Ann.*, **75** (1850), 316.
[7] Hibbert: *Ber.*, **39** (1906), 160.
[8] Landolt: *J. prakt. Chem.*, **84** (1861), 329.

Clear, colorless liquid; b.p. 80°; sp. gr. 1.523 at 15°; very slightly soluble in water; soluble in absolute alcohol, ether, or carbon bisulfide; inflammable in the air; combines explosively with halogens; reduces auric and mercuric chlorides and silver nitrate to the free metals. Reacts exothermically with methyl iodide.

Triethylstibine: $(C_2H_5)_3Sb$

(a) Prepared by the action of an alloy of potassium and antimony on ethyl iodide.[9]

(b) Distillation of triethylstibinic iodide with zinc yields triethylstibine.[10]

(c) Forms when antimony trichloride is treated with mercury diethyl.[11]

(d) When zinc diethyl is treated with antimony trichloride, triethylstibine is formed very readily.[12]

Colorless, mobile liquid; does not solidify even at —29°; b.p. 158° at 730 mm.; sp. gr. 1.3244; fumes and burns in the air; combines explosively with halogens. The stibine may be preserved under water; combines smoothly with bromine under water yielding the stibinic bromide. Reacts with fuming hydrochloric acid to form the stibinic chloride and hydrogen. Combines gradually with ethyl iodide.

Triamylstibine: $(C_5H_{11})_3Sb$

A small flask is filled to about ⅔ of its capacity with a mixture of sand and a potassium-antimony alloy, and sufficient amyl iodide is added to moisten it. Gradually a vigorous reaction commences which generates sufficient heat to volatilize the excess amyl iodide. The reaction mixture is cooled in an atmosphere of carbon dioxide, and the amylstibine is extracted with ether. Water is added to the extract, and the ether is removed by evaporation in the presence of carbon dioxide. The stibine remains as an oil protected from the air by the water which was added prior to evaporation.[13]

The triamylstibine may be distilled from the original reaction mixture in a manner analogous to that used in preparing triethyl-

[9] Löwig and Schweizer: *Ann.*, **75** (1850), 316.
[10] Buckton: *Quart. J. Chem. Soc.*, **13** (1861), 116.
[11] *Ibid.*, **16** (1863), 22.
[12] Hofmann: *Ann.*, **103** (1857), 357.
[13a] Berlé: *J. prakt. Chem.*, **65** (1855), 385.
[b] Berlé: *Ann.*, **97** (1856), 316.

stibine,[14] but under these conditions partial decomposition takes place.[15]

Triamylstibine is a transparent, slightly yellow liquid; sp. gr. 1.133 at 17°; insoluble in water; slightly soluble in alcohol; insoluble in ether. It combines additively with halogens but does not react with amyl iodide even at 100°. In the air, it fumes, but is not inflammable.

Phenyl-dimethylstibine: $C_6H_5Sb(CH_3)_2$

An ethereal solution of excess methylmagnesium iodide is treated with a similar solution of phenylstibinous chloride and then refluxed for 1.5 hours. After decomposition with water and drying with calcium chloride, evaporation of the ether yields an oil which is distilled under diminished pressure in the presence of carbon dioxide.[16]

Colorless, mobile oil, b.p. 112° at 16-18 mm., fumes in the air, oxidizes rapidly in solution, yields stibinic halides very readily when treated with halogens.

Phenyl-diethylstibine: $C_6H_5Sb(C_2H_5)_2$ Prepared from ethylmagnesium iodide and phenylstibinous chloride in ether solution.[17] Colorless liquid; b.p. 128° at 16-18 mm.; fumes in the air and oxidizes vigorously. The stibinic halides are formed by direct addition of halogen as in the case of the dimethyl analogue.

Methyl-diphenylstibine: $CH_3(C_6H_5)_2Sb$

Prepared from methylmagnesium bromide (15 g.) and diphenylstibinous chloride (25 g.) by the Grignard reaction.[18] Yield: 10-11 g. Colorless, viscous oil; b.p. 174-177° at 16-18 mm.; does not fume in the air, but undergoes oxidation very readily; forms no stibonium compounds with methyl or ethyl iodide even when heated for 10 hours at 100°.

Ethyl-diphenylstibine: $C_2H_5(C_6H_5)_2Sb$

Prepared from diphenylstibinous chloride (25 g.) by the Grignard reaction;[19] yield 10-11 g. Colorless, viscous oil; b.p. 190-

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[14] Cramer: *Jahrsb. Fort. Chem.*, (1855), 590.

[15a] Scheibler: *J. prakt. Chem.*, **64** (1855), 505.

[b] Ref. 13b, p. 318.

[16] Grüttner and Wiernik: *Ber.*, **48** (1915), 1759, used a crude phenylstibinous chloride which contained some diphenylstibinous chloride and found it necessary to fractionate the resulting oil.

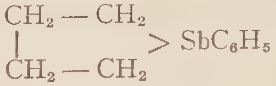
[17] Ref. 16, p. 1761.

[18] Ref. 16, p. 1762.

[19] Ref. 16, p. 1764.

192° at 16-18 mm.; fumes scarcely any in the air; oxidizes very readily; does not react with methyl or ethyl iodides even at 100°.

Cyclotetramethylene-phenylstibine:

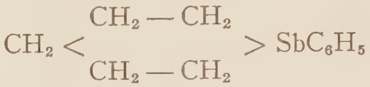


$$\left.\begin{array}{l} CH_2-CH_2 \\ | \\ CH_2-CH_2 \end{array}\right> SbC_6H_5$$

From 1,4-dibromobutane and phenylstibinous chloride by the Grignard reaction.[20]

Colorless, rather viscous oil; b.p. 156-158° at 20-22 mm.; oxidizes very readily in the air.

Cyclopentamethylene-phenylstibine:



$$CH_2 < \begin{array}{l} CH_2-CH_2 \\ \\ CH_2-CH_2 \end{array} > SbC_6H_5$$

From 1,5-dibromopentane and phenylstibinous chloride by the Grignard reaction.[21] Yield: 37 g. from 75 g. of phenylstibinous chloride. Colorless, viscous oil; b.p. 169-171° at 18-20 mm. Soluble in ether, benzene, carbon tetrachloride, hot alcohol; insoluble in water. Combines directly with oxygen and halogens but not with alkyl halides even at 100°. Decomposed by mercuric chloride.

Triphenylstibine: $(C_6H_5)_3Sb$

(a) From bromobenzene and antimony trichloride by the Grignard reaction.[22]

(b) A benzene solution of bromobenzene or chlorobenzene and antimony trichloride is treated with an excess of sodium.[23] The crude stibine which is obtained by evaporation of the benzene solution may be purified by recrystallization from light petroleum[24] instead of extraction with alcoholic hydrochloric acid. Yield 70%.

If an excess of sodium is not present the product is triphenylstibinic chloride or, if bromobenzene is used, a mixture of the stibinic chloride and bromide. Small amounts of di and tri phenyl stibinic chlorides are always formed as by-products.

[20] Grüttner and Krause: *Ber.*, **49** (1916), 442.

[21] Grüttner and Wiernik: *Ber.*, **48** (1915), 1484.

[22a] Ref. 3.

[b] Morgan and Micklethwait: *J. Chem. Soc.*, **99** (1911), 2290.

[23a] Michaelis and Reese: *Ber.*, **15** (1882), 2877.

[b] Ref. 5.

[c] Morgan and Vining: *J. Chem. Soc.*, **117** (1920), 779. By modifying the mode of procedure, the reaction may be controlled exactly, and large quantities may be made.

[24] May: *J. Chem. Soc.*, **97** (1910), 1957.

$$2SbCl_3 + 6C_6H_5Br + 8Na \rightarrow (C_6H_5)_3SbBr_2 + (C_6H_5)_3SbCl_2 + 4NaCl + 4NaBr$$

(c) Bromobenzene is heated with an alloy of sodium and antimony; the yield is smaller than in (b).[25]

(d) Mono or diphenylstibinous oxide when heated for 4 hours at 180-200° in an atmosphere of carbon dioxide yields triphenylstibine, which is extracted from the solid material with ether. Evaporation of the extract leaves an oil which solidifies and may be recrystallized from glacial acetic acid.[26]

$$3C_6H_5SbO \rightarrow (C_6H_5)_3Sb + Sb_2O_3$$

Colorless or slightly yellow, transparent plates; m.p. 46-48°, 48°, 48-50°, 53°; distills with some decomposition at 360°. May be recrystallized from glacial acetic acid or alcohol. Soluble in petroleum ether, ether, benzene, chloroform, carbon bisulfide; insoluble in alcohol, water, hydrochloric acid. Reacts readily with halogens to form stibinic halides; does not combine with methyl iodide even at 100°.

When heated with antimony trichloride, triphenylstibine yields a mixture of mono and di phenylstibinous chlorides; the latter, but not the former, may be isolated in a pure form from the reaction mixture.[27]

$$(C_6H_5)_3Sb + SbCl_3 \rightarrow C_6H_5SbCl_2 + (C_6H_5)_2SbCl$$

When refluxed in methyl alcoholic-hydrochloric acid, the tertiary stibine is converted into diphenylstibinous chloride.[28]

It is oxidized by alkaline hydrogen peroxide to diphenylstibinic acid; in neutral solutions triphenylstibinic oxide is formed;[29] after oxidation with permanganate in acid solution, a small quantity of triphenylstibinic hydroxide may be isolated.[30] The stibine reduces cupric and ferric chlorides in alcoholic or ether solution to cuprous and ferrous chlorides.

Tri-p-tolylstibine: $(4\text{-}CH_3C_6H_4)_3Sb$

(a) Pure p-bromotoluene and antimony trichloride are treated in benzene solution with excess sodium; the reaction commences spontaneously, and the flask must be cooled occasionally. After

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[25] Löloff: *Ber.*, **30** (1897), 2836.
[26] Schmidt: *Ann.*, **421** (1920), 242.
[27] Cf. Chap. III for a detailed discussion of this reaction.
[28] Schmidt: *Ann.*, **429** (1922), 140.
[29] Ref. 28, p. 141.
[30] Ref. 24, p. 1959.

8 hours, the reaction mixture is refluxed for a short while, filtered, and evaporated; the residual oil crystallizes readily.[31] In a later paper, the same authors recommend the use of 36 g. of antimony tribromide, 51 g. of pure p-bromotoluene and 50 g. of sodium in 4 volumes of benzene. After 2 or 3 days, the benzene solution is evaporated.[32] Yield 63%.

(b) From p-bromotoluene and antimony tribromide by the Grignard reaction; the residue obtained by evaporation of the ether solution is recrystallized from methyl alcohol.[33]

Large, colorless, transparent plates; m.p. 126°, 127.5°. Soluble in chloroform, benzene, ether; difficultly soluble in alcohol and petroleum ether. Adds halogens very readily; does not react with methyl iodide at 100°. Soluble in concentrated nitric and sulfuric acids but not in hydrochloric acid. Reduces cupric chloride in alcoholic solution. Forms a molecular compound with mercuric chloride, $(p\text{-}CH_3C_6H_4)_3Sb \cdot HgCl_2$, which decomposes in boiling alcohol to form p-tolylmercuric chloride.

Tri-o-tolylstibine: $(2\text{-}CH_3C_6H_4)_3Sb$

A solution of 36 g. of antimony tribromide and 51 g. of pure o-bromotoluene in 4 volumes of benzene is treated with 50 g. of sodium; the reaction mixture must be cooled at first. After 4 or 5 days, the insoluble material is filtered out and washed with benzene. Evaporation of the combined filtrates yields an oil which solidifies readily.[34]

If the o-bromotoluene is contaminated with the para isomer, the product contains some di-o-tolyl-p-tolylstibine, and the mixture is separated by conversion into the stibinic bromides which, after fractional crystallization, are reduced to the stibines in alcoholic ammonia with hydrogen sulfide.

Colorless, transparent needles; m.p. 79-80°; soluble in chloroform, benzene, ether, and petroleum ether; insoluble in alcohol. Yields a molecular compound with mercuric chloride, $(o\text{-}CH_3C_6H_4)_3Sb \cdot HgCl_2$, when treated in alcoholic solution with mercuric chloride; colorless plates, decomposes at 135°. This molecular compound does not decompose into o-tolylmercuric chloride when heated in alcoholic solution.

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[31] Michaelis and Genzken: *Ber.*, **17** (1884), 924.
[32] Michaelis and Genzken: *Ann.*, **242** (1887), 164.
[33] Ref. 3, p. 4622.
[34] Ref. 32, p. 176.

Di-o-tolyl-p-tolylstibine: $(2\text{-}CH_3C_6H_4)_2Sb(C_6H_4CH_3\text{-}4)$

Formed as a by-product in the preparation of tri-o-tolylstibine when the o-bromotoluene contains small amounts of the para isomer.[34] Colorless crystals, m.p. 110-112°. Reacts in alcoholic solution with mercuric chloride forming a molecular compound; colorless needles which melt with decomposition at 164-165°.

Tri-m-tolylstibine: $(3\text{-}CH_3C_6H_4)_3Sb$

m-Bromotoluene and antimony tribromide are treated in benzene solution with excess sodium; after 2-3 days the benzene solution is filtered and evaporated; the residue solidifies readily.[35] Yield 65%.

An attempt to prepare this substance from antimony trichloride and m-tolylmagnesium bromide in benzene failed; only tri-m-tolylstibinic hydroxychloride was obtained.[36]

Large, colorless plates; m.p. 67-68°. Crystallizes readily from a mixture of alcohol and ether. Adds halogens very readily. Soluble in ether, benzene, chloroform, and acetic acid; difficultly soluble in petroleum ether. Reacts with mercuric chloride to form $(3 - CH_3C_6H_4)_3Sb \cdot HgCl_2$, white crystals; melts with decomposition at 140°; soluble in chloroform but not in ether, alcohol, benzene, or petroleum ether. The substance yields m-tolylmercuric chloride when boiled with alcohol.

Tri-p-xylylstibine: $[2,5\text{-}(CH_3)_2C_6H_3]_3Sb$

(a) A solution of 24 g. of bromo-p-xylene and 3.5 g. of magnesium in 50 cc. of ether is treated gradually with 9 g. of antimony trichloride dissolved in 20 cc. of ether. After refluxing for 4 hours, the mixture is decomposed with water and filtered. The dry residue is extracted with hot benzene; the extract yields 7.25 g. of the crystalline material when evaporated.[37]

(b) Larger yields are obtained by refluxing bromo-p-xylene and antimony trichloride with excess sodium in benzene.[38]

Short, transparent needles, m.p. 174.5°. Readily soluble in benzene, cold chloroform, or boiling glacial acetic acid; moderately soluble in hot acetone; and less soluble in ether or alcohol. Reduces thallic chloride.

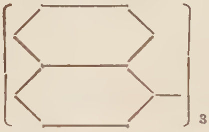
[35a] Ref. 31, p. 925.
[b] Ref. 32, p. 184.
[36] Challenger and Pritchard: *J. Chem. Soc.,* 125 (1924), 869.
[37] Goddard: *J. Chem. Soc.,* 123 (1923), 1170.
[38] *Ibid.,* 124 (1923), 2317.

Tri-m-xylylstibine: $[2,4\text{-}(CH_3)_2C_6H_3]_3Sb$

(a) A benzene solution of 4-bromo-m-xylene and antimony trichloride is treated with sodium; the mixture is warmed slightly to start the reaction and is then allowed to stand over night. The insoluble matter is extracted with hot benzene; the oil obtained by evaporation of the benzene solution solidifies when poured into absolute alcohol.[39] Yield: 57%.

(b) From 4-bromo-m-xylene and antimony trichloride by the Grignard reaction.[39] Yield: 19%.

Long needles; m. p. 148°; soluble in cold chloroform, acetone, light petroleum, or pyridine; moderately soluble in alcohol. Combines readily with halogens; reacts with mercuric chloride in alcohol to form a double salt—$[(CH_3)_2C_6H_3]_3Sb \cdot HgCl_2$; fine needles, m.p. 158°.

Tri-α-naphthylstibine:  Sb. A benzene solution of antimony trichloride is added to an ethereal solution of α-naphthylmagnesium bromide.[40] M.p. 218°. Sparingly soluble in most organic solvents.

Tri-p-anisylstibine: $(4\text{-}CH_3OC_6H_4)_3Sb$

(a) p-Bromoanisole and antimony trichloride are treated in benzene solution with sodium; after 24 hours a small quantity of sodium is added, and the mixture is refluxed. The residue obtained by evaporation of the benzene solution contains some bromoanisole which is removed by distillation with steam; the residue is redissolved in a mixture of benzene and chloroform and the solution is evaporated.[41] Yield: 68 g. from 200 g. of p-bromoanisole.

(b) p-Bromoanisole is heated with a sodium-antimony alloy. Yield 10%.[41]

Colorless rhombohedra; m.p. 180.5-181°. Readily soluble in chloroform; less soluble in benzene and toluene; difficultly soluble in alcohol, ether, ethyl acetate, glacial acetic acid, carbon bisulfide; insoluble in petroleum ether. Decomposed by concentrated hydrochloric acid.

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[39] Ref. 38, p. 2319.

[40] Challenger and Pritchard: *J. Chem. Soc.*, 125 (1924), 869.

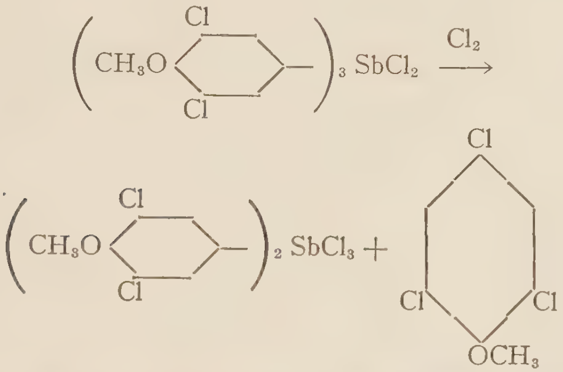
[41] Ref. 25, p. 2835.

$$(CH_3OC_6H_4)_3Sb + 3HCl \rightarrow CH_3OC_6H_5 + SbCl_3$$

Forms a double salt with mercuric chloride: $(CH_3OC_6H_4)_3Sb \cdot HgCl_2$, sinters at 235-240°, decomposes at 285° without melting; insoluble in ordinary solvents; when boiled in alcohol, decomposition takes place with the formation of p-anisylmercuric chloride.

Decomposed by chlorine even in cold chloroform solution instead of forming a stibinic chloride as most tertiary stibines do.

$$(CH_3OC_6H_4)_3Sb \xrightarrow{Cl_2} (CH_3OC_6H_4)_3SbCl_2 \xrightarrow{Cl_2}$$



Adds bromine and iodine without decomposing; reduces cupric chloride.

$$(CH_3OC_6H_4)_3Sb + 2CuCl_2 \rightarrow (CH_3OC_6H_4)_3SbCl_2 + Cu_2Cl_2$$

Tri-p-phenetylstibine: $(p\text{-}C_2H_5OC_6H_4)_3Sb$

Prepared from p-bromophenetole and antimony trichloride in benzene solution by the action of excess sodium.[42] Yield is small.

Needles, m.p. 82-83°; readily soluble in benzene, chloroform, ether, alcohol, and petroleum ether. Decomposed by hot aqueous hydrochloric acid into phenetole and antimony trichloride. Reacts in alcoholic solution with mercuric chloride to form a double salt: $(C_2H_5OC_6H_4)_3Sb \cdot HgCl_2$; white, crystalline powder; insoluble in nearly all solvents; softens 205-210°, decomposes at 225°; when refluxed in alcohol, it decomposes forming p-phenetylmercuric chloride. The behavior toward halogens and cupric chloride is similar to that of tri-p-anisylstibine.

Tri-m-amino-triphenylstibine: $(3\text{-}NH_2C_6H_4)_3Sb$

(a) Tri-m-nitro-triphenylstibinic hydroxide (2 g.) is added to 100 cc. of boiling alcohol containing 5 g. of zinc dust and 0.8 g. of ammonium chloride; after ½ an hour the crude product is precipitated by filtering into 100 cc. of ice water, and it is purified by reprecipitation from aqueous hydrochloric acid solution by means of ammonia.[43] During the reduction some decomposition occurs whereby part of the antimony is split off; this destructive reduction becomes more pronounced when tin and hydrochloric acid are used.

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[42] Ref. 25, p. 2841.

Colorless crystals; decomposes indefinitely at about 80°; difficultly soluble in water and organic solvents. A crystalline trihydrochloride is precipitated from a solution of the base in dilute hydrochloric acid by concentrated acid.

(b) m-Aminophenylstibinous oxide is heated for about 1 hour at 120-125° in a current of carbon dioxide. The tertiary stibine is extracted by acetone and obtained as an oil, which gradually solidifies, by treating the extract with water. Recrystallization from alcohol yields colorless needles,[44] m.p. 124°.

Tri-m-amino-triphenylstibine exists in two forms:[44] α—obtained by precipitating the stibine from aqueous hydrochloric acid with ammonia, sinters about 80°; β—obtained by recrystallization from alcohol, m.p. 124°. The α form contains 0.5 molecule of water, while the β form is anhydrous. The difference between the two is not solely due to the water content, because this water may be removed in a vacuum desiccator without altering the sintering point, i.e., 80°. The two substances are interconvertible:

$$\alpha \underset{\text{Precipitation from hydrochloric acid solution}}{\overset{\text{Recrystallization from alcohol, or heating at 100°}}{\rightleftarrows}} \beta$$

Tri-p-acetylamino-triphenylstibine: $(4\text{-}CH_3CONHC_6H_4)_3Sb$

A suspension of p-acetylaminophenylstibinous oxide (50 g.) in methyl alcohol (400 cc.) is refluxed in an atmosphere of carbon dioxide for 3 hours, and then filtered while hot. A part of the stibine crystallizes from the filtrate. An additional quantity is obtained by extracting the residue which is secured by evaporation of the alcoholic mother liquor with acetone containing some water and diluting the extract with water. In a similar manner, still

[43] Ref. 22b, p. 2292.

[44] Schmidt: *Ann.*, 421 (1920), 242.

more may be extracted from the solid which was filtered out of the hot alcohol after the period of refluxing.[45] Yield 23 g.

Di-p-acetylamino-diphenylstibinous oxide is converted into the tertiary stibine only at 180°.

Three modifications of this compound exist:

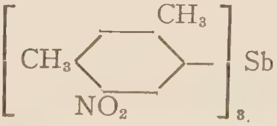
α—$(CH_3CONHC_6H_4)_3Sb \cdot \frac{1}{2}H_2O$. Obtained in needles by recrystallization from methyl alcohol. Sinters at 205°, melts 270°. Only about 2% soluble in hot methyl alcohol.

β—$(CH_3CONHC_6H_4)_3Sb$. M.p. 268°. Obtained from the α form by recrystallization from anhydrous acetone or by refluxing with benzene.

γ—$(CH_3CONHC_6H_4)_3Sb \cdot \frac{2}{3}H_2O$. Sinters at 225°. Crystallizes when water is added to a solution of the α form in moist acetone. When a solution of either the β or γ forms in a large volume of hot methyl alcohol is cooled, the α modification crystallizes.

Oxidation of the α modification in methyl alcohol solution with hydrogen peroxide yields tri-p-acetylamino-triphenylstibinic oxide which is finally precipitated by the addition of water $(p\text{-}CH_3CONHC_6H_4)_3SbO \cdot 4H_2O$. M.p. 200°. After recrystallization from anhydrous methyl alcohol the material melts at 250°. The oxide is converted into a stibinic chloride by alcoholic hydrochloric acid. However, oxidation of the stibine in alkaline solution yields di-p-acetylamino-diphenylstibinic acid.

Tri-5-nitro-tri-m-xylylstibine:



(a) A boiling solution of 2 g. of tri-5-nitro-tri-m-xylylstibinic nitrate in 200 cc. of absolute alcohol and 20 cc. of ammonia water is treated with hydrogen sulfide for 6 hours; the stibine separates upon cooling.[46]

(b) Tri-6-bromo-tri-5-nitro-tri-m-xylylstibinic oxide (1.8 g.) dissolved in 40 cc. of hot absolute alcohol is added to a boiling solution of 1.4 g. of sodium thiosulfate in 25 cc. of water. After 30 minutes, the solution is cooled; the product separates at once.[46]

Small needles; m.p. 192-193°; may be recrystallized from alcohol, or chloroform-petroleum ether mixtures.

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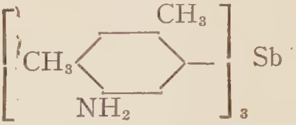
[45] Ref. 28, p. 132.
[46] Ref. 38, p. 2320.

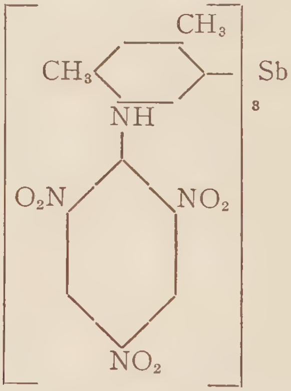
Tri-5-amino-tri-m-xylylstibine:



Five grams of the mixture of nitration products, obtained by the action of fuming nitric acid on tri-m-xylylstibine,[47] is added to 400 cc. of boiling absolute alcohol containing 3.5 g. of ammonium chloride, 20 cc. of ammonia water and 22 g. of zinc dust. The boiling is continued for 8 hours; at the end of each hour, 5 g. of zinc dust is added. The hot solution is filtered into 3 l. of ice-water, and the product which separates is reprecipitated from aqueous hydrochloric acid by the addition of aqueous ammonia.[48] Yield: 97%.

Brownish-pink powder; darkens at 112°, melts indefinitely at 123-124°; may be recrystallized from a mixture of chloroform and light petroleum; soluble in aqueous hydrochloric acid. When warmed with benzoyl chloride in pyridine solution, the stibine yields tri-5-benzoylamino-tri-m-xylylstibine (m.p. 99°).

Tri-picryl-tri-5-amino-tri-m-xylylstibine:



The amino stibine (2 g.) dissolved in a small quantity of 10% hydrochloric acid is added to 75 cc. of alcohol containing 3 g. of picryl chloride and 8 g. of sodium acetate, and the mixture is kept at 30° for 15 minutes; the crude product (3.9 g.) which separates is extracted with water, dried, and precipitated from chloroform solution with light petroleum.[49] Bronze, crystalline powder; sinters at 178°, darkens but does not melt even at 290°. Soluble in alcoholic potash, and the carmine solution slowly deposits scarlet crystals of the potassium salt.

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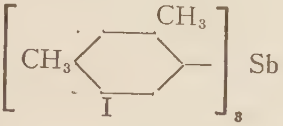
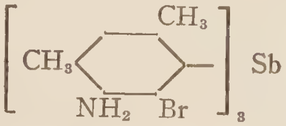
[47] Cf. Tri-5-nitro-tri-m-xylylstibinic nitrate.
[48] Ref. 38, p. 2321.
[49] Ref. 38, p. 2322.

Tri-5-iodo-tri-m-xylylstibine:



A solution of 1 g. of tri-5-amino-tri-m-xylylstibine in 7 cc. of HCl (sp. gr. 1.19) and 200 cc. of water is diazotized and treated with 1.5 g. of potassium iodide in 20 cc. of water. The crude product (1.5 g.) which separates after the reaction mixture has been kept on a water bath for 3 hours, is recrystallized 5 times from a mixture of chloroform and petroleum ether.[50] Brownish-red, crystalline powder; m.p. 153°.

Tri-6-bromo-tri-5-amino-tri-m-xylylstibine:



The corresponding bromo-nitro-xylylstibinic oxide (1.7 g.) is reduced in alcoholic ammonia with ammonium chloride and zinc dust;[51] yield 0.85 g. M.p. 123-124°.

B. Stibinous Oxides and Salts.

Antimonials of this type cause marked irritation when they come in contact with the skin and mucous membranes; some of them, e.g., phenylstibinous chlorides, produce painful burns.

1. Primary.

Phenylstibinous oxide: C_6H_5SbO

(a) A solution of phenylstibinic acid (25 g.) in hydrochloric acid (100 cc., sp. gr. 1.18), after dilution with methyl alcohol (200 cc.) and water (90 cc.), is cooled, treated with sodium iodide (0.5 g.) and saturated with sulfur dioxide. After several hours, the addition of ice and excess ammonia water precipitates the stibinous oxide which, after drying, is a voluminous powder sintering at 153-4°. It may be purified by diluting a solution of it in a small quantity of glacial acetic acid, and adding this solution, after filtration, to cold aqueous ammonia.[52]

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[50] Ref. 38, p. 2321.

[51a] Cf. Tri-5-amino-tri-m-xylylstibine.

[b] Ref. 49.

(b) When a glacial acetic acid (50 cc.) solution of diphenylstibinous oxide (5 g.) is refluxed for 20 minutes in an atmosphere of carbon dioxide, cooled and treated with cold ammonia water, the primary stibinous oxide precipitates.[53]

(c) An aqueous suspension of phenylstibinous chloride is treated with aqueous sodium carbonate: after some time the solid is filtered out and washed with hot water. The crude, dry material is extracted with hot alcohol; the extract yields a crystalline product upon evaporation.[54]

Insoluble in most organic solvents and practically so in alkalies; readily soluble in formic and acetic acids probably due to the formation of a formate or acetate. Fuming nitric acid oxidizes it violently. Decomposes gradually at 100° forming diphenylstibinous oxide; at 180-200° triphenylstibine forms. Converted into stibinous halides by halogen acids.

Phenylstibinous Salts:

Chloride: $C_6H_5SbCl_2$

(a) The oxide is extracted with a cold mixture of acetic and hydrochloric acids; the extract, after standing for some time in a freezing mixture deposits the chloride in a crystalline condition.[55]

(b) Although phenylstibinous chloride is formed when triphenylstibine is heated with antimony trichloride,[56] it can not be isolated in a pure state from the reaction mixture due to the ease with which it decomposes.

$$2C_6H_5SbCl_2 \rightarrow (C_6H_5)_2SbCl + SbCl_3$$

Colorless crystals; m.p. 62°; readily soluble in methyl and ethyl alcohols; decomposes gradually into diphenylstibinous chloride.

Iodide: $C_6H_5SbI_2$

(a) Precipitates when a concentrated solution of sodium iodide is added to a solution of the oxide in a mixture of acetic and hydrochloric acids.[57]

[52] Ref. 26, p. 217.

[53] Ref. 28, p. 143.

[54] Hasenbäumer: *Ber.*, **31** (1898), 2912.

[55] Ref. 26, p. 219.

[56a] Cf. Chap. III for a discussion of this reaction.

[b] Morgan and Vining, Ref. 23c, p. 781, carried out this reaction on a large scale.

[57] Ref. 26, p. 218.

(b) A cold solution of 10 g. of phenylstibinic acid in 40 cc. of hydrochloric acid (sp. gr. 1.126) is treated with a solution of 10 g. of stannous chloride in 30 cc. of hydrochloric acid (sp. gr. 1.126), and a concentrated aqueous solution sodium iodide is added till a yellow precipitate no longer forms. The precipitate is oily at first but soon becomes crystalline; it is washed with dilute hydrochloric acid and dried in a desiccator.[57]

Yellow crystals, m.p. 69°. Sparingly soluble in methyl and ethyl alcohols, acetone, carbon bisulfide, benzene, and ether; may be recrystallized from glacial acetic acid. When impure it is not stable in the air; it gradually becomes red due to the formation of antimony tri-iodide.

When alcoholic solutions of these stibinous halides are treated with water partial hydrolysis takes place and oxyhalides are formed.

Sulfide: C_6H_5SbS. A warm solution of either the oxide or the chloride in alcoholic ammonia is saturated with hydrogen sulfide.[58] The crude product is precipitated by acidification with hydrochloric acid; it is recrystallized from alcohol. Crystals; m.p. 65°.

3-Aminophenylstibinous oxide: $3\text{-}NH_2C_6H_4SbO$

(a) 3-Nitrophenylstibinic acid (5 g.) is reduced by warming with 18 g. of tin and an excess of 4N-hydrochloric acid containing a small amount of glacial acetic acid; the product is precipitated from the filtered solution by the addition of excess caustic soda.[59] Yield: 2.6 g.

(b) A cold paste of m-aminophenylstibinous chloride hydrochloride in water is treated with an excess of cold ammonia water; after a short time the solid is collected, washed well with water and dried in a desiccator.[60]

A white (yellow-May) powder; sinters at 170°. Although the freshly precipitated material is fairly soluble in water, the dry product is quite insoluble. Insoluble in alkali; slightly soluble in alcohol; readily soluble in dilute acids. Gradually decomposes when heated above 100°. m-Aminophenylstibinous oxide is oxidized by the air in the presence of alkali but there is a distinct tendency for part of the antimony to be eliminated from the organic compound during the process. The presence of some substance, e.g., tartaric acid, which readily reacts with antimony oxide accentuates this tendency. Thus, if a dilute alkaline solution of the above oxide and some tartaric acid is aerated, the oxidation product is m,m′-diaminodiphenylstibinic acid.

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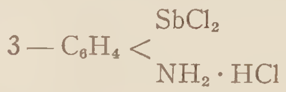
[58] Ref. 54, p. 2913.
[59] May: *J. Chem. Soc.,* **101 (1912), 1035.**
[60] Ref. 26, p. 225.

3-Aminophenylstibinous chloride hydrochloride:

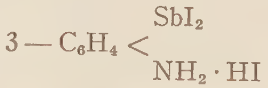


$$3-C_6H_4<\begin{matrix}SbCl_2\\NH_2\cdot HCl\end{matrix}$$

A mixture of 30 g. of 3-nitrophenylstibinic acid and 95 g. of stannous chloride is treated gradually, with occasional cooling, with 230 cc. of saturated alcoholic hydrochloric acid; the product crystallizes from the clear solution and is washed with concentrated hydrochloric acid. It may be recrystallized from acidified aqueous methyl alcohol.[61] This reduction may be carried out in concentrated hydrochloric acid, but in this case the product is contaminated with colored impurities.

Colorless needles; m.p. 215°, (218°) with darkening; fairly soluble in water and methyl alcohol; less soluble in ethyl alcohol; insoluble in acetone, ether and benzene. In aqueous solution it gradually decomposes forming antimony oxide and diamino-diphenylstibinous chloride; hydrochloric acid stabilizes the solution. After saturation of a fresh solution with hydrogen sulfide, sodium acetate precipitates a yellow sulfide.

3-Aminophenylstibinous iodide hydroiodide:



$$3-C_6H_4<\begin{matrix}SbI_2\\NH_2\cdot HI\end{matrix}$$

An acidified solution of the chloride yields a yellow, crystalline precipitate of the iodide when treated with sodium iodide. M.p. 160°; difficultly soluble in water; readily soluble in warm alcohol.[62]

4-Acetylaminophenylstibinous chloride: 4-$CH_3CONHC_6H_4SbCl_2$

(a) A cold solution of 4-acetylaminophenylstibinic acid (50 g.) in concentrated hydrochloric acid (100 cc.) and glacial acetic acid (350 cc.) is treated with a solution of stannous chloride (34 g.) in concentrated hydrochloric acid (150 cc.) and a trace of iodine. The reduction product crystallizes gradually, and after filtration, it is washed with a mixture of acetic and hydrochloric acids (1 : 1) and then with ether. This substance is the hydrochloride of the

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[61a] Ref. 26, p. 223.
[b] Ger. Pat. 268,451.
[62] Ref. 26, p. 225.

stibinous chloride, $4\text{-}CH_3CONHC_6H_4SbCl_2 \cdot HCl \cdot H_2O$; colorless crystals sintering at 125°. It is not very stable, however, and even in the presence of methyl alcohol, it decomposes into hydrochloric acid and the acetylamino stibinous chloride which is a colorless, stable, crystalline substance melting at 200°.[63]

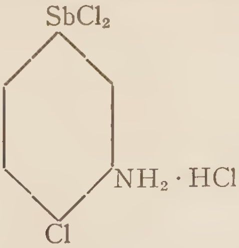
(b) A solution of 3 g. of di-p-acetylaminodiphenylstibinous oxide in 30 cc. of acetic acid, after being maintained at 70° for 1 hour, yields the hydrochloride of the stibinous chloride, cf. above, when cooled and treated with 60 cc. of cold concentrated hydrochloric acid.[64] Yield: 1.5 g. If the acetic acid is replaced with 100% formic acid, the reaction takes place at room temperature.

4-Acetylaminophenylstibinous oxide:

$$4\text{-}CH_3CONHC_6H_4SbO \cdot H_2O$$

A cold, methyl alcohol suspension of 50 g. of the stibinous chloride is treated with 600 cc. of cold N-ammonium hydroxide.[65] An amorphous powder; sinters at 180°; somewhat soluble in glacial acetic acid; insoluble in methyl alcohol and water; the freshly precipitated material is slightly soluble in water. When heated, or allowed to stand in acetic acid solution containing tartaric acid decomposition occurs with the separation of antimony oxide.

3-Amino-4-chlorophenylstibinous chloride hydrochloride:



A mixture of 33 g. of 3-nitro-4-chlorophenylstibinic acid and 95 g. of stannous chloride is treated gradually with 250 cc. of saturated alcoholic hydrochloric acid. The reduction product crystallizes from the clear solution and is washed with concentrated hydrochloric acid, glacial acetic acid, and ether.[66] White needles, m.p. 153°, readily soluble in methyl alcohol and very dilute hydrochloric acid. Cold, dilute ammonium hydroxide precipitates the stibinous oxide from a methyl alcohol solution of the chloride; the oxide, unlike the m-aminophenylstibinous oxide, is quite insoluble in water even when freshly precipitated. Also, it decomposes with the liberation of part of its antimony less readily than the unchlorinated oxide.

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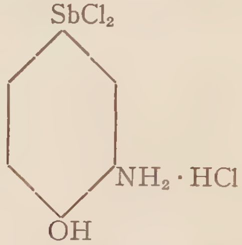
[63] Ref. 28, p. 129.
[64] Ref. 28, p. 139.
[65] Ref. 28, p. 130.
[66] Ref. 26, p. 231.

3-Amino-4-hydroxyphenylstibinous chloride hydrochloride:



A solution of 24 g. of 3-nitro-4-hydroxyphenylstibinic acid in 60 cc. of saturated alcoholic hydrochloric acid is added gradually to a cold (— 5°) solution of 60 g. of stannous chloride in 45 cc. of saturated alcoholic hydrochloric acid. The temperature is allowed to rise slowly to 22°, and then the reaction mixture is placed in an ice mixture for 2 days; the reduction product crystallizes slowly. After washing with cold, concentrated hydrochloric acid and drying, it may be purified by precipitation from methyl alcohol solution with ether.[67]

M.p. 165-170°—depending upon the manner of heating. Aqueous solutions of this substance decompose with the separation of antimony trioxide. Converted by cold ammonia water into the corresponding oxide, and oxidized by hydrogen peroxide in the presence of ammonium hydroxide to the amino-hydroxyphenylstibinic acid.

p-Tolylstibinous chloride: $p\text{-}CH_3C_6H_4SbCl_2$

Tri-p-tolylstibine (10 g.), when heated with antimony trichloride (12 g.) and xylene in a sealed tube at 245° for 48 hours, is dearylated.[68] Hasenbäumer claims to have isolated p-tolylstibinous chloride from the reaction mixture by distillation in a stream of carbon dioxide as a crystalline solid, m.p. 93.5°. As it was later shown that phenylstibinous chloride, when prepared in an analogous manner, can not be isolated in a pure condition, it is possible that the tolylstibinous chloride is also impure.

The material obtained in this way is soluble in alcohol, ether and petroleum ether; reacts with alkali carbonates to form an oxide;

[67] Ref. 28, p. 150.

[68] Ref. 54, p. 2914.

combines with chlorine to form a stibinic chloride; reacts with ammonium sulfide to form a sulfide (long needles). The stibinic chloride hydrolyzes readily, forming a stibinic acid.

2. Secondary.

Diphenylstibinous oxide: $[(C_6H_5)_2Sb]_2O$

(a) Dry phenylstibinous oxide is heated on a water bath in the presence of carbon dioxide for 4 hours. Extraction with warm alcohol leaves a residue of antimony oxide, and the extract, when evaporated slowly, yields crystalline diphenylstibinous oxide.[69]

(b) To a solution of 5 g. of phenylstibinous oxide in 50 cc. of acetic acid, 25 cc. of 20% tartaric acid solution is added. Gradually, crystals, probably the stibinous tartrate, separate, which, when dissolved in methyl alcohol, are converted into diphenylstibinous oxide by the addition of ammonia water.[70]

(c) A solution of triphenylstibine (9 g.) in methyl alcohol (150 cc.) and saturated alcoholic hydrochloric acid (30 cc.) is refluxed for 1 hour in an atmosphere of carbon dioxide, cooled and treated with excess caustic soda. By evaporation of an ether extract of the oil which separates, a good yield of diphenylstibinous oxide is secured as an oil; the latter may be crystallized from alcohol.[71]

(d) When digested with aqueous sodium carbonate, the stibinous chloride yields the oxide.[72]

Colorless crystals, m.p. 78-80°. Hydrochloric acid precipitates diphenylstibinous chloride, m.p. 68°, from an acetic acid solution of the oxide. Hypophosphorus reduces the oxide to a yellow compound—probably tetraphenyldistibine $(C_6H_5)_2Sb\text{-}Sb(C_6H_5)_2$. Fuming nitric acid oxidizes the oxide violently, but hydrogen peroxide in alkaline solution produces diphenylstibinic acid. Crystallization of the oxide from a hot acetic acid solution yields the stibinous acetate. When shaken with dilute sulfuric acid or alcoholic oxalic acid, an ethereal solution of diphenylstibinous oxide yields precipitates of a sulfate and oxalate respectively. Refluxing an acetic acid or alcoholic hydrochloric acid solution of diphenylstibinous oxide causes decomposition to take place and phenylstibinous oxide can be isolated.

[69] Ref. 26, p. 234.
[70] Ref. 26, p. 235.
[71] Ref. 28, p. 14.
[72] Michaelis and Günther: *Ber.*, 44 (1911), 2318.

Diphenylstibinous chloride: $(C_6H_5)_2SbCl$

(a) Obtained by the addition of hydrochloric acid to an acetic acid solution of the oxide.

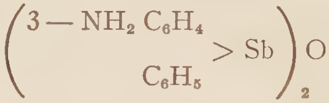
(b) After extracting the mixture of mono and diphenylstibinous chlorides, which forms when triphenylstibine and antimony trichloride are heated, with warm dilute hydrochloric acid, the residue consists of pure diphenylstibinous chloride.[73] Yield: 3 g. from 25 g. of triphenylstibine.

White crystals; m.p. 68°; soluble in alcohol, benzene and ether; insoluble in water; not hydrolyzed by water; converted into the stibinous oxide by digestion with aqueous sodium carbonate. Combines directly with chlorine, forming diphenylstibinic chloride.

Diphenylstibinous sulfide: $[(C_6H_5)_2Sb]_2S$. An alcoholic solution of the stibinous oxide is treated with hydrogen sulfide and then evaporated. The crystalline sulfide is recrystallized from alcohol.[72] Long, white needles, m.p. 69°.

Diphenylstibinous acetate: $(C_6H_5)_2SbOCOCH_3$ crystallizes from a hot glacial acetic acid solution of the oxide.[74] Colorless needles; m.p. 132°; readily soluble in methyl alcohol; hydrolyzed by water.

3-Amino-diphenylstibinous oxide:



$$\left(\begin{matrix}3-NH_2\,C_6H_4\\ C_6H_5\end{matrix}>Sb\right)_2O$$

The hydrochloride of 3-amino-diphenylstibinic acid (43 g.), dissolved in 300 cc. of methyl alcohol, is reduced at room temperature with sulfur dioxide. The addition of 20 g. of hydrochloric acid (sp. gr. 1.123) and 100 cc. of water precipitates the by-products, and the stibinous oxide is precipitated from the filtered and cooled solution by the addition of alkali.[75] Slightly colored powder; sinters at 70°; insoluble in alkali.

Di-3-amino-diphenylstibinous chloride dihydrochloride:

$$(3\text{-}HCl\cdot NH_2C_6H_4)_2SbCl$$

When a solution of 8 g. of m-aminophenylstibinous chloride hydrochloride in 500 cc. of water is boiled, antimony trioxide separates. After several hours the precipitate is removed, and the residue obtained by evaporation of the filtrate is extracted with water. Con-

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[73a] Ref. 72, p. 2317.

[b] Grüttner and Wiernik: *Ber.*, **48** (1915), 1749.

[74] Ref. 28, p. 140.

[75] Ger. Pat. 269,206.

centrated hydrochloric acid precipitates colorless needles of the secondary stibinous chloride from the extract.[76] M.p. 215°; easily soluble in water.

Di-3-amino-diphenylstibinous hydroxide: $(3\text{-}NH_2C_6H_4)_2SbOH$

Precipitates when an aqueous solution of the stibinous chloride hydrochloride is treated with alkali.[77] Colorless; sinters indefinitely at about 70°; soluble in alcohol and acetone but not in ethyl acetate.

Di-4-acetylamino-diphenylstibinous chloride hydrochloride:

$$(4\text{-}CH_3CONHC_6H_4)_2SbCl \cdot HCl$$

Tri-p-acetylamino-triphenylstibine (4 g.) is suspended in a small amount of methyl alcohol and treated with alcoholic hydrochloric acid till it dissolves. After an excess of the alcoholic acid has been added the secondary stibinous chloride crystallizes gradually from the cold solution;[78] yield 3 g. M.p. 135°. This substance is not stable, and the loosely bound hydrochloric acid causes hydrolysis of the acetyl group.

Di-4-acetylamino-diphenylstibinous hydroxide:

$$(4\text{-}CH_3CONHC_6H_4)_2SbOH \cdot 1\tfrac{1}{2}H_2O$$

A suspension of 5.2 g. of the freshly prepared chloride in 10 cc. of methyl alcohol is treated at 0° with 5N-sodium hydroxide solution until it is alkaline (*ca* 7 cc.). The clear solution is treated with water until it is permanently turbid, filtered and placed in an ice bath. The crystals are washed with dilute methyl alcohol and reprecipitated from methyl alcohol with water.[79]

Colorless, small crystals; m.p. 130°; slightly soluble in methyl alcohol and less soluble in ethyl alcohol. In acetic or formic acid solution, the oxide decomposes, and p-acetylaminophenylstibinous oxide may be isolated in good yields.

C. Stibino Compounds.

Stibinobenzene: $C_6H_5Sb = SbC_6H_5$

(a) A solution of 12 g. of sodium hypophosphite in 15 cc. of acetic acid is added to a solution of 4 g. of phenylstibinous oxide in 80 cc. of acetic acid and 80 cc. of acetone, and the mixture is maintained at 65° for 2-3 hours. Stibinobenzene gradually separates as a brown precipitate which is washed with methyl alcohol and dried *in vacuo*.[80]

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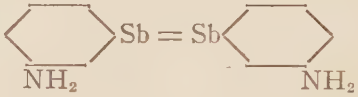
[76] Ref. 26, p. 239.
[77] Ref. 26, p. 240.
[78] Ref. 28, p. 136.
[79] Ref. 28, p. 137.

(b) A solution of phenylstibinic acid in the calculated quantity of aqueous sodium hydroxide is treated, with stirring, with an aqueous solution of sodium hydrosulfite. After several hours at 30° the yellowish-brown precipitate is collected and dried. In order to remove the sulfur containing impurities the crude material is refluxed with a mixture of alcohol and benzene (1 : 1) and some copper powder. The solution, upon evaporation, yields stibinobenzene as a yellow powder.[81]

Darkens and sinters at 160°. Insoluble in ordinary solvents; the product obtained in (b) is said to be soluble in glacial acetic acid and hot chloroform. Oxidizes very readily; in the air the substance soon turns yellow and occasionally takes fire; concentrated nitric acid oxidizes it explosively, and ammoniacal hydrogen peroxide oxidizes it to phenylstibinic acid.

3,3′-Diamino-stibinobenzene:



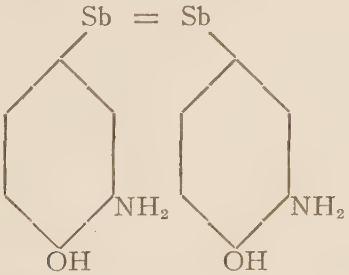
(a) In an inert atmosphere, a paste of 3.2 g. of the hydrochloride of 3-aminophenylstibinous chloride and 10 cc. of water is treated with a solution of 10 g. of sodium hypophosphite in 25 cc. of water and 10 cc. of hypophosphorous acid (sp. gr. 1.15). The reaction commences at room temperature but is preferably carried out at 50°. Upon cooling, the deep red solution yields a hypophosphite or phosphite of the stibino compound as a red-brown precipitate, which redissolves when more water is added. By pouring into an excess of dilute soda solution, the diamino-stibinobenzene separates as a dark brown flocculent precipitate.[82]

(b) A solution of 3-aminophenylstibinous chloride hydrochloride in dilute aqueous sodium hydroxide is treated with an aqueous alkaline solution of sodium hydrosulfite and magnesium chloride. The stibino compound separates slowly at room temperature but rapidly at a slightly higher temperature. The yellow diamino-stibinobenzene is purified by dissolution in tartaric acid and precipitation with alcohol.[83]

[80] Ref. 26, p. 221.
[81] Ger. Pat. 268,451.
[82] Ref. 26, p. 230.
[83] Ger. Pat. 268,451.

Above 120° it sinters to a black mass. Easily soluble in acetic acid, pyridine, and hydrochloric acid; excess hydrochloric acid precipitates a hydrochloride, and sulfates precipitate an acid sulfate from a solution of the hydrochloride. Very susceptible to oxidation. If a solution of the base in dilute hydrochloric acid is allowed to stand, decomposition gradually takes place and ultimately metallic antimony separates.

3,3′-Diamino-4,4′-dihydroxystibinobenzene:



(a) 3-Amino-4-hydroxyphenylstibinous chloride hydrochloride (2.2 g.) is treated with 4 cc. of acetic acid, 7 cc. of water, and a solution of 6.6 g. of sodium hypophosphite in 18 cc. of water and 6.6 cc. of hypophosphorous acid (sp. gr. 1.15). The solution is filtered rapidly and warmed in an atmosphere of carbon dioxide at 30° for 45 minutes. The solution becomes dark red and the hypophosphite or phosphite of the stibino base separates as a red solid. After cooling in ice for several hours the latter is collected and dried rapidly. When a solution of the product in ammonium hydroxide or dilute sodium hydroxide is treated with ammonium chloride the free stibino base precipitates. After washing, the dark brown solid is dried in a vacuum desiccator.[84]

(b) A solution of 3.1 g. of 3-nitro-4-hydroxyphenylstibinic acid in 50 cc. of water containing 0.5 g. of sodium hydroxide is added to a solution of 20 g. of sodium hydrosulfite in 400 cc. of water containing 1.7 g. of sodium hydroxide. The initial precipitate is redissolved by the addition of more alkali. The stibino base separates gradually at 40° as a reddish-brown solid which is collected and washed in an inert atmosphere.[85]

3,3′-Diamino-4,4′-dihydroxystibinobenzene, the antimony analogue of arsphenamine base, is a dark brown powder which is very susceptible to oxidation. Soluble in dilute caustic soda and hydrochloric acid; such solutions are quite unstable. Concentrated hydrochloric acid precipitates a brown dihydrochloride from a solution of the base in dilute hydrochloric acid. Sulfates precipitate an acid sulfate from solutions of the hydrochloride. Oxidized by alkaline hydrogen peroxide to 3-amino-4-hydroxyphenylstibinic acid.

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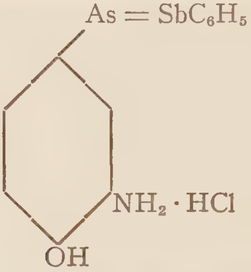
[84] Ref. 28, p. 151.

[85] Ger. Pat. 268,451.

D. Arseno-Stibino Compounds.

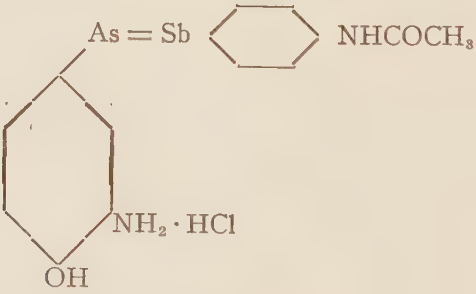
3-Amino-4-hydroxyarseno-stibinobenzene hydrochloride:



A solution of 1.9 g. of 3-amino-4-hydroxyphenylarsine in 30 cc. of methyl alcohol and 1 cc. of 10N-alcoholic hydrochloric acid is mixed in the absence of oxygen with a methyl alcoholic solution of phenylstibinous chloride; the solution rapidly becomes brown. When the reaction mixture is poured into 500 cc. of ether the arseno-stibino compound precipitates; it is washed with absolute ether and dried in a vacuum.[86]

Brown, amorphous powder; soluble in methyl alcohol, water and caustic alkalies. An aqueous solution yields a precipitate of a difficultly soluble sulfate when treated with dilute sulfuric acid.

3-Amino-4-hydroxyarseno-4′-acetamino-stibinobenzene hydrochloride:



[86a] Ehrlich and Karrer: *Ber.*, 46 (1913), 3567.
[b] Ger. Pat. 269,743.

A solution of 1.64 g. of 4-acetaminophenylstibinous iodide in 40 cc. of glacial acetic acid is treated with a solution of 0.8 g. of 3-amino-4-hydroxyphenylarsine in methyl alcoholic hydrochloric acid; the product is precipitated from the dark brown solution by pouring into ether.[87]

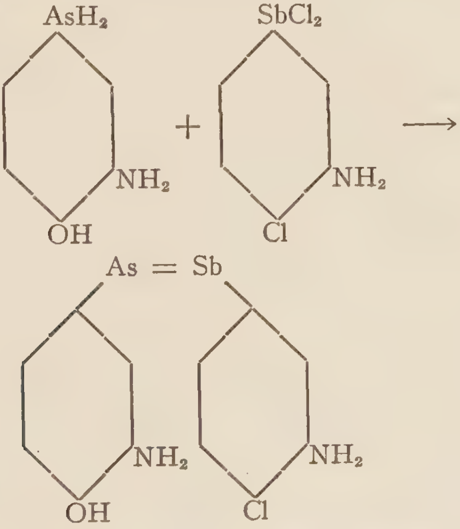
Amorphous, dark brown powder; readily soluble in water, methyl alcohol and caustic soda.

4-Hydroxy-arseno-stibinobenzene: 4-$HOC_6H_4As = SbC_6H_5$

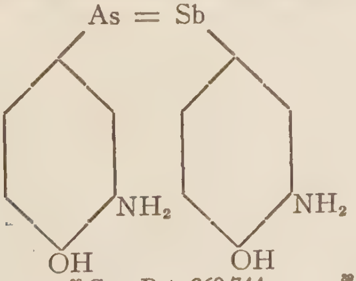
Condensation of 4-hydroxyphenylarsine and phenylstibinous oxide; brown solid.[88]

3,3′-Diamino-4-hydroxy-4′-chloro-arseno-stibinobenzene:

Prepared by condensing 3-amino-4-chlorophenylstibinous chloride dissolved in dilute aqueous hydrochloric acid with 3-amino-4-hydroxyphenylarsine.[89]



3,3′-Diamino-4,4′-dihydroxy-arseno-stibinobenzene:



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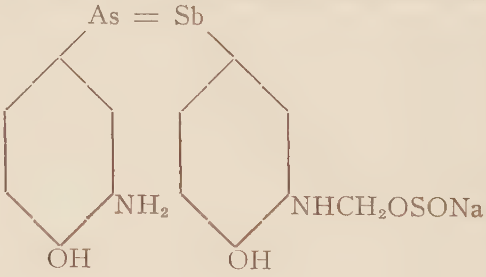
[87] Ref. 86a, p. 3564. [88] Ger. Pat. 269,744. [89] Ref. 26, p. 232.

Solutions prepared by dissolving 12.8 g. of 3-nitro-4-hydroxyphenylarsonic acid and 15 g. of the corresponding stibinic acid separately in 300 cc. of water and 8.5 cc. of 40% sodium hydroxide solution at 45° are added simultaneously with stirring to a cold solution of 300 g. of sodium hydrosulfite in 1.7 l. of water, and the temperature is gradually raised to 68°. The arseno-stibino base separates gradually; after 1.5 hours it is collected on a filter in an inert atmosphere and washed with water and then with methyl alcohol.[90] The dried base is insoluble in neutral solvents.

The dihydrochloride of the arseno-stibino base may be prepared by suspending the base obtained above in methyl alcohol and adding 12 cc. of a 29% methyl alcohol solution of hydrochloric acid. The dark brown solution is filtered and poured into either anhydrous ether or concentrated hydrochloric acid; the dihydrochloride precipitates. The product is a brownish-yellow amorphous powder readily soluble in water; the aqueous solution is distinctly acid. The addition of sodium hydroxide to such a solution regenerates the free base which redissolves in excess caustic.

A sodium sulfoxylate derivative of the arseno-stibino compound may be obtained by dissolving 1.9 g. of the above dihydrochloride in 6 cc. of methyl alcohol and adding 2 cc. of 37.5% sodium sulfoxylate solution. After neutralizating with aqueous sodium carbonate, the solution is filtered and poured into 400 cc. of a mixture of anhydrous alcohol and ether (1:1). The product is dried *in vacuo*. There is no evidence given as to which of the amino groups reacts with the sulfoxylate, but the product may be represented by the following formula:—



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[90] U. S. Pat. 1,422,294.

Chapter 8.

Organic Derivatives of Pentavalent Antimony.

A. Stibinic Acids.

Examples of Preparation of Stibinic Acids by the Diazo Reaction.

(a)[1] A solution of 28 g. of aniline in 180 cc. of 5N-hydrochloric acid and 200 cc. of water is diazotized and placed in a 10 l. beaker. After some cracked ice has been added, a solution of 48 g. of antimony oxide in 150 cc. of hydrochloric acid (sp. gr. 1.18) is introduced with continuous stirring; a voluminous precipitate forms. When excess sodium hydroxide solution (650 cc. of 20% alkali) is added, the solution foams and fills the entire container. After the foam has subsided, the brown insoluble matter which contains some unchanged antimony oxide is filtered out, and the crude phenylstibinic acid is precipitated from the filtrate, by acidification, as a slightly colored, voluminous solid which is filtered out and dried.

The crude material, which contains some inorganic antimony compounds and colored by-products, is dissolved by gentle warming in 150 cc. of hydrochloric acid (sp. gr. 1.18) and treated with 150-200 cc. of water in order to precipitate the brown impurities. The yellow filtrate is treated with an excess of solid ammonium chloride and fuming hydrochloric acid in order to precipitate the double salt $C_6H_5SbCl_4 \cdot NHCl_4$ as a voluminous, yellow solid. The latter is collected on a filter, washed free from inorganic antimonials with concentrated hydrochloric acid and added to 1 l. of water; the chloride undergoes hydrolysis and phenylstibinic acid precipitates. After washing thoroughly with water, the material is dissolved in dilute sodium hydroxide, filtered and reprecipitated with mineral acid. After washing and drying, the solid is again washed with water to remove any soluble impurities which were occluded by the original gelatinous precipitate and redried.

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[1] Schmidt: *Ann.*, **421** (1920), 188.

(b)[2] A solution of 28 g. of aniline in 75 cc. of water and 150 cc. of 5N-hydrochloric acid is diazotized and treated with 150 cc. of hydrochloric acid (sp. gr. 1.126). While cold, a solution of 45 g. of antimony oxide in 150 cc. of hydrochloric acid (sp. gr. 1.126) is added. The voluminous, crystalline double salt $C_6H_5N_2Cl \cdot SbCl_3$ is filtered out, suspended in water, and while thoroughly cooled, is treated with an excess of dilute sodium hydroxide. The isolation and purification is the same as in (a).

(c)[3] o-Nitraniline (13.8 g.) in 100 cc. of 5N-nitric acid is diazotized, and the solution, which is cooled by the addition of cracked ice, is treated with 40 cc. of 5N-sodium hydroxide and a solution of 33 g. of tartar emetic. With continuous stirring, sodium hydroxide solution is added until a vigorous evolution of nitrogen commences—usually 40 cc. of 5N-alkali is sufficient. When the diazo compound can no longer be detected, the system is made strongly alkaline and is then acidified and warmed in order to completely precipitate the stibinic acid which is filtered out and dried. The yellow-brown powder is freed from antimony oxide by means of concentrated hydrochloric acid and then dissolved in alcoholic hydrochloric acid. By cautiously adding water, the dark colored impurities may be precipitated, and the filtrate from this precipitate yields a yellow, flocculent precipitate of o-nitrophenylstibinic acid when diluted with more water.

1. Primary Stibinic Acids.

Phenylstibinic acid: $[3(C_6H_5SbO_2)H_2O]2H_2O$

(a) From diazotized aniline and antimony trioxide in the presence of alkali.[4] Purified by conversion into the ammonium chloride double salt of phenylstibinic chloride which is subsequently hydrolyzed by water.

(b)[5] An aqueous suspension of the antimony trichloride double salt of benzene diazonium chloride is treated with alkali; the reaction proceeds more smoothly than in (a). The isolation and purification of the product are the same as in (a).

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[2] Ref. 1, p. 189.
[3] Ref. 1, p. 205.
[4a] Ref. 1.
[b] U. S. Pat. 1,260,707.
[c] Ger. Pat. 254,421.
[d] Eng. Pat. 16,350. (1912).
[5] Ref. 1, p. 189.

(c) The impure phenylstibinous chloride obtained by heating triphenylstibine and antimony trichloride is suspended in ether and treated with chlorine; the oily addition product, when hydrolyzed with aqueous ammonia, yields some insoluble matter—diphenylstibinic acid. From the ammoniacal solution, hydrochloric acid precipitates phenylstibinic acid.[6] Yield: 26 g. from 57 g. of triphenylstibine.

White, non-melting solid; insoluble in water or alcohol; slightly soluble in acetone; soluble in warm glacial acetic acid, tetrachloroethane, chloroform, and amyl acetate; soluble in cold mixtures of alcohol with chloroform, benzene, or ether. Solutions in mixed solvents deposit fine crystals slowly. Converted into the stibinic chloride by concentrated hydrochloric acid. Soluble in dilute alkalies; the behavior of the stibinic acids toward alkalies is discussed in Chapter 4. Hydrogen sulfide precipitates a yellow phenylstibinic sulfide from an acetic acid solution of the acid. Barium chloride precipitates a white barium phenylstibinate from an ammoniacal solution of the acid.

2-Nitrophenylstibinic acid: $[3(2\text{-}NO_2C_6H_4SbO_2) \cdot 2H_2O]3H_2O$
A diazotized solution of o-nitraniline in 5N-nitric acid is partially neutralized, after the addition of some ice, with 5N-sodium hydroxide, and a solution of tartar emetic is added. While thoroughly agitated, 5N-caustic solution is gradually added until a vigorous evolution of nitrogen commences. When the reaction is complete, the mixture is made distinctly alkaline and then acid; the complete separation of the stibinic acid is hastened by warming. The crude, dried powder is freed from antimony oxide by extraction with cold concentrated hydrochloric acid and is further purified by adding some water to a solution of it in alcoholic-hydrochloric acid in order to precipitate the dark colored impurities. The addition of more water to the filtrate from these impurities precipitates the pure nitrophenylstibinic acid.[7]

o-Nitrophenylstibinic acid is a brownish yellow powder, which does not melt below 285°. Sparingly soluble in methyl or ethyl alcohols, alcohol-chloroform mixtures, or hot acetic acid. Soluble in dilute alkali in which permanent neutrality is rapidly attained. Converted into oily clumps by warm concentrated hydrochloric acid;

[6a] May: *J. Chem. Soc.,* **101** (1912), 1033.
[b] Morgan and Micklethwait: *J. Chem. Soc.,* **99** (1911), 2295.
[c] Hasenbäumer: *Ber.,* **31** (1898), 2913.
[7] Ref. 1, p. 205.

it does not dissolve. Easily soluble in methyl alcohol-hydrochloric acid mixtures, excess acid precipitates the stibinic chloride.

3-Nitrophenylstibinic acid: $[3(3\text{-}NO_2C_6H_4SbO_2) \cdot 2H_2O]3H_2O$

(a) Phenylstibinic acid is added gradually to an excess of cool nitric acid (sp. gr. 1.515) or it is nitrated in sulfuric acid solution at a slightly higher temperature (40-55°) with a mixture of nitric and sulfuric acids.[8] The crude product, which is precipitated by diluting the nitration mixture with ice water, is dissolved in aqueous sodium hydroxide and reprecipitated with acetic or hydrochloric acid. For further purification the acid may be converted into the stibinic chloride which is reconverted into the acid by hydrolysis.

(b) From diazotized m-nitraniline and tartar emetic in slightly acid solution;[9] the yield is small.

Slightly yellow powder; does not melt below 290°; soluble in hot acetic acid and mixtures of alcohol with chloroform or carbon bisulfide; insoluble in tetrachlorethane; readily soluble in dilute alkali. A solution of the acid in warm hydrochloric acid yields the stibinic chloride upon cooling. When heated with chloroform and phosphorus pentabromide in a sealed tube at 100-110°, m-bromonitrobenzene is formed; yield 70%.

4-Nitrophenylstibinic acid: $[3(4\text{-}NO_2C_6H_4SbO_2) \cdot 2H_2O] \cdot 3H_2O$

The double salt $4\text{-}NO_2C_6H_4N_2Cl \cdot SbCl_3$, prepared from diazotized p-nitraniline and antimony trichloride, is suspended in water, treated with a slight excess of sodium hydroxide and acidified with hydrochloric acid. The crude, dry product is washed with concentrated hydrochloric acid, dissolved in alcoholic hydrochloric acid, and reprecipitated with water.[10] Chrome-yellow powder; decomposes without melting at about 300°.

2-Aminophenylstibinic acid: $2\text{-}NH_2C_6H_4SbO_2 \cdot H_2O$

(a) A solution 5 g. of 2-nitrophenylstibinic acid in 150 cc. of water and 15 cc. of 5N-sodium hydroxide is stirred for 10-15 minutes with an excess of ferrous hydroxide which has been previously separated by centrifuging from the solution in which it was precipitated. The suspension is again centrifuged, and the liquid, after clarification with carbon, is treated with salt and acidified with

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[8a] Morgan and Micklethwait: *J. Chem. Soc.,* **99** (1911), 2296.
[b] Ref. 1, p. 202.
[c] Ger. Pat. 287,709.
[9] Ref. 1, p. 205.
[10] Charrier: *Gazz. chim. ital.,* **52,** II (1922), 16.

acetic acid. After drying, the precipitate is extracted with cold water to remove the occluded salt.[11]

(b) A suspension of the nitro acid in methyl alcohol is treated with titanous chloride; the amino acid is precipitated with hydrochloric acid, washed with salt solution, and the mineral acid is eliminated with sodium acetate.[11]

(c) Breinl and Nierenstein[12] claim to have secured this compound from o-chloroaniline and magnesium in dry ether solution by treatment with antimonic acid. Such a reaction is quite unexpected, and the properties of the product do not agree with those given by Macallum.

Brownish powder; darkens above 150°; very slightly soluble in water; soluble in alkalies, methyl alcohol, warm glycerine and dilute acetic acid; yields o-iodoaniline when treated with potassium iodide and dilute acetic acid.

2-Acetaminophenylstibinic acid: $2\text{-}CH_3CONHC_6H_4SbO_2 \cdot H_2O$

Attempts to prepare this substance from mono acetyl-o-phenylenediamine by the diazo reaction failed, but it is formed when a moderately concentrated neutral solution of the amino acid is acetylated with an excess of acetic anhydride at 0°. Does not melt below 250°; slightly soluble in formic acid, warm glycerine, dilute acetic acid, and alkalies.[13]

3-Aminophenylstibinic acid: $[3(3\text{-}NH_2C_6H_4SbO_2)H_2O]4H_2O$

(a) A suspension of 3-aminophenylstibinous chloride hydrochloride in ice and water is treated with excess ammonium hydroxide and the calculated quantity of hydrogen peroxide. Acetic acid precipitates the stibinic acid from the resulting solution; excess acetic acid redissolves the precipitate. The crude product is converted into the stibinic chloride by concentrated hydrochloric acid, and an aqueous solution of the chloride is decomposed with the calculated quantity of sodium hydroxide.[14]

(b) May oxidized 3-aminophenylstibinous oxide with alkaline hydrogen peroxide but was unable to isolate a stibinic acid.[15]

Darkens but does not melt when heated; insoluble in methyl and ethyl alcohols; readily soluble in acids and alkalies. Forms colored Schiff bases when treated with aromatic aldehydes.

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[11] Macallum: *J. Soc. Chem. Ind.*, **42** (1923), 468T.

[12] Breinl and Nierenstein: *Ann. Trop. Medicine and Parasit.* (1908-09), II, 381.

[13] Macallum: *J. Soc. Chem. Ind.*, **42** (1923), 468T.

[14a] Ref. 1, p. 226.

[b] Ger. Pat. 270,488.

[15] May: *J. Chem. Soc.*, **101** (1912), 1033.

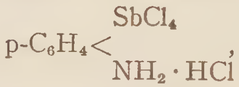
4-Acetylaminophenylstibinic acid:

$4\text{-}CH_3CONHC_6H_4SbO_2 \cdot nH_2O$

Mono acetyl-p-phenylenediamine (15 g.) in 14.7 g. of sulfuric acid and 100 cc. of water is diazotized. After the addition of a hydrochloric acid solution of antimony oxide, an excess of alkali is added. When the vigorous reaction is over, the filtrate is almost neutralized with dilute sulfuric acid and saturated with carbon dioxide to precipitate the impurities and unchanged antimony oxide. The filtrate yields the sodium salt of the stibinic acid when it is saturated with sodium chloride. The precipitate is freed from occluded sodium chloride by dissolving in methyl alcohol and evaporating the extract. The resulting sodium p-acetylaminophenylstibinate dissolves in water, forming a neutral solution from which acids precipitate the free stibinic acid.[16]

4-Aminophenylstibinic acid (stibanilic acid):

$[3(4\text{-}NH_2C_6H_4SbO_2) \cdot 3H_2O]4H_2O$

4-Acetylaminophenylstibinic acid (30 g.) is hydrolyzed by heating in caustic potash solution (235 cc. of 1.8NKOH) at 90° for 1 hour; the product is precipitated by the addition of acetic acid. The crude acid is converted into the hydrochloride of the stibinic chloride,  $p\text{-}C_6H_4<\begin{matrix} SbCl_4 \\ NH_2 \cdot HCl \end{matrix}$, by treatment with concentrated hydrochloric acid. When decomposed with the calculated quantity of aqueous sodium hydroxide, the chloride yields the free acid.[17]

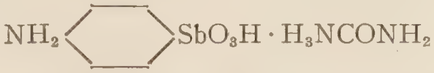
p-Aminophenylstibinic acid is a colorless powder which is insoluble in organic solvents but readily soluble in dilute caustic soda. When warmed with potassium iodide and dilute sulfuric acid, p-iodoaniline is formed.

[16a] U. S. Pat. 1,260,707.
[b] Ger. Pat. 254,421.
[c] Eng. Pat. 16,350. (1912).

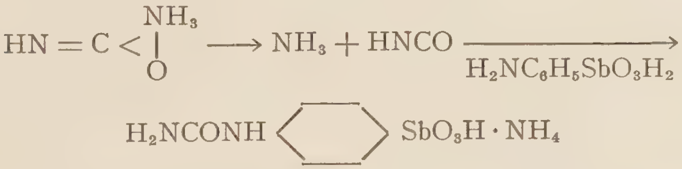
[17a] Schmidt: *Ann.*, **429** (1922), 145.
[b] Ger. Pat. 270,488—the acetyl group is removed by hydrolysis in 5% sodium hydroxide solution.
[c] Breinl and Nierenstein: Ref. 12, p. 379, state that when aniline is heated with antimony trichloride, p- or o-aminophenylstibinous chloride is formed depending upon the experimental conditions. Although these substances were not isolated, they claim to have obtained the corresponding stibinic acids by oxidation of the reaction mixture. These results could not be obtained by subsequent investigators.

The sodium salt is precipitated from a solution of the acid in aqueous sodium hydroxide by the addition of alcohol; this is the antimony analogue of atoxyl.

The urea salt of stibanilic acid is obtained by adding urea to a warm aqueous suspension of stibanilic acid until a clear solution is obtained; the latter is concentrated as a water bath, and the salt is precipitated by the addition of alcohol.[18]



In a recent paper [19] it is stated that the substance obtained by this reaction is not a urea salt of stibanilic acid but a substituted urea which is formed in the following manner:



$$HN = C < \begin{matrix} NH_3 \\ | \\ O \end{matrix} \longrightarrow NH_3 + HNCO \xrightarrow[H_2NC_6H_5SbO_3H_2]{}$$

Carbethoxy-p-aminophenylstibinic acid:

$4\text{-}C_2H_5O_2C \cdot NHC_6H_4SbO_2 \cdot H_2O$

An alkaline solution of p-aminophenylstibinic acid is treated with ethyl chlorocarbonate; the product is precipitated by acidification with hydrochloric acid.[20]

Benzenesulfonyl-p-aminophenylstibinic acid:

$4\text{-}C_6H_5SO_2NHC_6H_4SbO_2 \cdot H_2O$

An alkaline solution of p-aminophenylstibinic acid is treated at 60° with benzene sulfonyl chloride; the product is precipitated by acidification with hydrochloric acid.[20]

N-Phenylglycinamide-p-stibinic acid:

$H_2N \cdot OCCH_2NHC_6H_4SbO_2 \cdot H_2O$

An alkaline solution of p-aminophenylstibinic acid is refluxed for 2 hours with chloroacetamide. The crude product, which is precipitated by acidification, is redissolved in dilute caustic and precipitated again with dilute acetic acid.[21] The sodium salt of this acid is analogous to tryparsamide.

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[18] Brahmachari: *Indian J. Med. Research,* **10** (1922), 508.

[19] Brahmachari and Das: *Ibid.,* 12 (1924), 423.

[20] Ref. 18, p. 509.

[21] Ref. 18, p. 511.

Allyl-thio-carbamino-p-aminophenylstibinic acid (4-stibonophenyl-allyl thio urea): $4\text{-}C_3H_5NH \cdot CS \cdot NHC_6H_4SbO_2 \cdot H_2O$

Sodium p-aminophenylstibinate and allylthiocarbamide are kept at room temperature in methyl alcohol solution for 24 hours. The solution is diluted with water and acidified.

Yellowish white, amorphous powder; soluble in sodium hydroxide but not in sodium carbonate.[22]

4-Hydroxyphenylstibinic acid: $[3(4\text{-}HOC_6H_4SbO_2)H_2O]6H_2O$

(a) Prepared from diazotized p-aminophenol and antimony trioxide in the presence of alkali. The crude material which is obtained by acidification of the alkaline reaction mixture is dark brown. While still moist the product is dissolved in cold concentrated hydrochloric acid, and isolated as the pyridine double salt of the stibinic chloride by addition of a hydrochloric acid solution of pyridine. The stibinic acid which precipitates when the double salt is decomposed in cold water is dissolved in caustic soda, decolorized with carbon and precipitated by the addition of acid.[23]

(b) A solution of 10.9 g. of p-aminophenol in 14.7 g. of sulfuric acid and 100 cc. of water is diazotized, treated with a hydrochloric acid solution of antimony oxide and with excess sodium hydroxide. After the reaction ceases, the solution is saturated with carbon dioxide, and the filtrate from the precipitated by-products and unchanged antimony oxide is saturated with sodium chloride. Acidification with dilute sulfuric acid yields the oxy stibinic acid.[24]

p-Hydroxyphenylstibinic acid is a colorless powder which darkens at high temperatures but does not melt even at 270°. It is sparingly soluble in alcohol and, when freshly precipitated, is soluble in hot water; the aqueous solution gives a violet color with ferric chloride. Soluble in sodium hydroxide, and hydrochloric acid (1.17); after standing, an acid solution gives a test for inorganic antimony. The solid material also decomposes gradually; after long standing, even in a stoppered flask, the acid and its sodium salt have a distinct odor of phenol.

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[22] Ref. 18, p. 512.
[23] Ref. 17a, p. 147.
[24a] U. S. Pat. 1,260,707.
[b] Ger. Pat. 254,421.
[c] Eng. Pat. 16,350. (1912).

The pyridine double salt, cf. above, is a yellow, stable substance. M.p. 176°.

Carboxy-methylene-oxyphenyl-4-stibinic acid (4-stibono-phenoxyacetic acid): $4\text{-}HO_2C \cdot CH_2OC_6H_4SbO_2 \cdot H_2O$

An alkaline solution of p-hydroxyphenylstibinic acid is treated at 60° with chloroacetic acid; after 3 hours the product is precipitated by acidification with hydrochloric acid.[25]

4-Anisylstibinic acid: Analysis is not reported.

Prepared from p-anisidine by the method used in the case of phenylstibinic acid.[26] This substance is somewhat less stable than the majority of the stibinic acids and can hardly be freed from the odor of anisole. It is not readily soluble in concentrated hydrochloric acid, but the addition of a small quantity of hydrochloric acid to a suspension of the material in methyl alcohol dissolves it. Excess hydrochloric acid precipitates a crystalline, yellow chloride which is very deliquescent and which readily decomposes with the elimination of the antimonial group.

4-Ethoxyphenylstibinic acid (p-phenetylstibinic acid):

$$[3(4\text{-}C_2H_5OC_6H_4SbO_2)H_2O] \cdot 2H_2O$$

(a) Prepared from diazotized phenetidine and antimony trioxide in the presence of alkali. The crude material is purified by stirring it with a hydrochloric acid solution of ammonium chloride in order to obtain a double salt of the stibinic chloride. When a cold methyl alcoholic solution of the latter, after decolorization with carbon, is diluted with water, the stibinic acid precipitates; it is then reprecipitated from alkaline solution by means of sulfuric acid.[27]

p-Ethoxyphenylstibinic acid is a colorless powder which has a slight odor of phenetole and which, while not melting even at 270°, darkens at high temperatures. Slightly soluble in methyl alcohol or chloroform but readily soluble in acetic acid, dilute sodium hydroxide, or mixtures of chloroform and methyl or ethyl alcohols or of benzene and alcohol. Hydrochloric acid converts the stibinic acid into a stibinic chloride which, like p-anisylstibinic chloride, is not stable.

4-Chlorophenylstibinic acid: $[3(4\text{-}ClC_6H_4SbO_2) \cdot 2H_2O]3H_2O$

(a) From p-chloroaniline by the diazo reaction, cf. phenylstibinic acid. The final purification involves the hydrolysis of the stibinic chloride which separates from a hydrochloric solution of the stibinic acid.[28]

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[25] Ref. 18, p. 510.

[26] Ref. 1, p. 213.

[27a] Ref. 17a, p. 148.

[b] Fargher and Gray: *J. Pharm. and Exper. Therap.*, 18 (1921), 354.

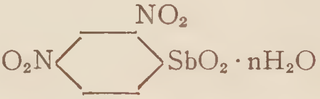
(b) The yellow double salt, $4\text{-}ClC_6H_4N_2Cl \cdot SbCl_3$, which is prepared from 50 g. of p-chloroaniline and 84 g. of antimony trichloride is suspended in 1.5 l. of water and treated with 150 g. of sodium hydroxide solution (sp. gr. 1.47). The insoluble matter is removed by filtration and washed with warm dilute caustic soda; the crude stibinic acid is precipitated from the filtrate by acidification. It is purified by conversion into the stibinic chloride and hydrolysis of the latter.[29]

Colorless powder; soluble in mixtures of alcohol with carbon bisulfide, chloroform, or benzene, from which it may be obtained in a crystalline condition.

4-Bromophenylstibinic acid: $4\text{-}BrC_6H_4SbO_2 \cdot nH_2O$

Prepared from diazotized p-bromoaniline and antimony trioxide in the presence of alkali. The reaction mixture is decolorized with carbon, made nearly neutral to litmus with dilute sulfuric acid, filtered from a small amount of dark precipitate and made neutral to Congo Red with dilute acid. The stibinic acid separates as a pale buff colored precipitate.[30]

2,4-Dinitrophenylstibinic acid:



$O_2N\left\langle\overset{NO_2}{\qquad}\right\rangle SbO_2 \cdot nH_2O$

2,4-Dinitraniline is diazotized and treated with tartar emetic in neutral or slightly acid solution.[31] Brown powder; explodes when heated.

3-Nitro-4-acetylaminophenylstibinic acid:

$3\text{-}NO_2\text{-}4\text{-}CH_3CONHC_6H_3SbO_2 \cdot nH_2O$

Anhydrous sodium 4-acetylaminophenylstibinate (113 g.) is dissolved in 300 g. of glacial acetic acid and cooled to — 2 to — 10°. After 800 g. of concentrated sulfuric acid has been added, a mixture of 100 g. of sulfuric acid and 25.4 g. of nitric acid (sp. gr. 1.515) is added gradually while the temperature is kept below 0°. Dilution with ice water, after several hours, yields the crude nitration product which is purified by precipitation from alkaline solution with

[28] Ref. 1, p. 207.
[29] Ger. Pat. 261,825.
[30] Fargher and Gray: *J. Pharm. and Exper. Therap.*, 18 (1921), 354.
[31] Ger. Pat. 296,940.

acids.[32] Yellowish-brown powder; decomposes on heating without melting.

3-Nitro-4-chlorophenylstibinic acid:

$$[3(3\text{-}NO_2\text{-}4\text{-}ClC_6H_3SbO_2)2H_2O]3H_2O$$

Dissolve 28 g. p-chlorophenylstibinic acid in 200 cc. concentrated sulfuric acid at a temperature below 25°, cool, and nitrate below 5° with a mixture of 4.2 cc. of nitric acid (sp. gr. 1.515) and 5 cc. of sulfuric acid. The mass is stirred for an hour after the nitrating acids have been added and is then poured onto ice. The crude product is purified as in the case of 3 nitrophenylstibinic acid.[33]

3-Nitro-4-chlorophenylstibinic acid is an almost colorless powder which does not melt below 285°. Readily soluble in warm methyl and ethyl alcohols; it is not precipitated from a dilute alcohol solution by water. Readily soluble in dilute alkalies and hydrochloric acid.

3-Nitro-4-hydroxyphenylstibinic acid:

$$[3(3\text{-}NO_2\text{-}4\text{-}HOC_6H_3SbO_2)\cdot 2H_2O]5H_2O$$

(a) The 3-nitro-4-chlorophenylstibinic acid, obtained by nitration of 56 g. of p-chlorophenylstibinic acid, is dissolved in sodium hydroxide and reprecipitated with hydrochloric acid. After filtration and washing, the moist nitro acid is heated in a water bath with 75 cc. of caustic potash (1:1). After some hours the potassium salt separates as a red precipitate, which is augmented by cooling and treatment with alcohol. The potassium salt is purified by reprecipitation from water solution with alcohol and is then converted into the free acid by acidification of an aqueous solution.[34]

(b) 3-Nitro-4-acetylaminophenylstibinic acid (35 g.) is heated with 300 g. of aqueous potassium hydroxide (sp. gr. 1.30) till ammonia ceases to be evolved. The product is precipitated by acidification with dilute sulfuric acid.[35]

3-Nitro-4-hydroxyphenylstibinic acid is a brownish-yellow powder which darkens when heated above 230°. Readily soluble in methyl alcohol, and the alcoholic solution merely becomes opalescent when diluted with water. Readily soluble in hot acetic acid, warm concentrated hydrochloric acid, and dilute alkalies. A hydrochloric acid solution when cooled, deposits a stable crystalline stibinic chloride in small quantities; the addition of ammonium chloride produces a crystalline, stable double salt.

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[32] Ger. Pat. 259,875; 287,709.

[33a] Ref. 1, p. 208.

[b] Ger. Pat. 262,236.

[34a] Ref. 1, p. 212.

[b] Ger. Pat. 262,236.

[35] Ger. Pat. 259,875.

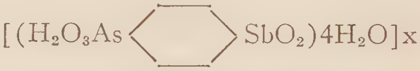
3-Amino-4-hydroxyphenylstibinic acid:

$3\text{-}NH_2\text{-}4\text{-}HOC_6H_3SbO_2 \cdot nH_2O$

(a) A cold solution of 30.8 g. of 3-nitro-4-hydroxyphenylstibinic acid in 160 cc. of water and 4 g. of sodium hydroxide is reduced with a solution of 65 g. of sodium hydrosulfite in 200 cc. of water and 2 g. of sodium hydroxide. The red color disappears, and the amino acid separates as a white precipitate; the excess hydrosulfite is destroyed by aeration.[36]

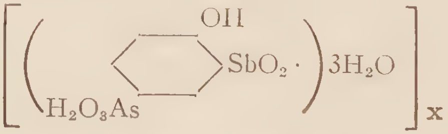
(b) The nitro acid may also be reduced in aqueous solution with sodium amalgam.[36]

White powder which darkens even in the dry state; decomposes without melting when heated; insoluble in neutral solvents but readily soluble in acids and alkalies.

4-Arsono-phenylstibinic acid: 

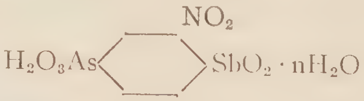
4-Aminophenylarsonic acid (arsanilic acid) is diazotized and treated with tartar emetic in slightly alkaline solution. The crude product is purified by conversion into the pyridine double salt of the stibinic chloride and hydrolysis of the latter. From 21.7 g. of arsanilic acid, 25 g. of the stibinic acid can be obtained as a colorless powder.[37] The substance may also be prepared by treating diazotized stibanilic acid with an alkali arsenite.

2-Hydroxy-5-arsonophenylstibinic acid:



3-Amino-4-hydroxyphenylarsonic acid is diazotized and treated with tartar emetic in alkaline solution. The crude product is purified in the same manner as the preceding compound. Slightly colored powder.[38]

2-Nitro-4-arsonophenylstibinic acid:



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[36] Ger. Pat. 270,488.

[37] Schmidt: *Ber.,* **57B** (1924), 1143.

[38] Ref. 37, p. 1147.

3-Nitro-4-aminophenylarsonic acid is diazotized and treated with tartar emetic in neutral or slightly acid solution.[39] Brown powder.

B. Preparation of Neutral Salts of Primary Aryl Stibinic Acids.

A neutral solution of a stibinic acid (1 mol.) in alkali (¼-⅓ mol.) is evaporated to dryness or precipitated with alcohol or saturated salt solution, and the crude neutral salt is extracted from the precipitate with methyl alcohol. Upon evaporation of the extract a pure neutral salt is obtained.[40]

The product is usually a mixture of the salts of the complex stibinic acid ($ArSbO_2 \cdot nH_2O$) and the hydrated acid $ArSbO_3H_2$, although in some instances it contains only a salt of the complex acid.

TABLE X[41]

NEUTRAL SODIUM ARYLSTIBINATES

Sodium Salt of	*Composition of Salt*
3 or 4-acetylaminophenylstibinic acid	$(CH_3CONHC_6H_4SbO_2)_3OHNa$
4-bromophenylstibinic acid	$(BrC_6H_4SbO_2)_3OHNa$ 36.8% and $BrC_6H_4SbO_3HNa$ 63.2%
4-ethoxyphenylstibinic acid	$(C_2H_5OC_6H_4SbO_2)_3OHNa$ 29.75% and $C_2H_5OC_6H_4SbO_3HNa$ 70.25%
phenylstibinic acid	$(C_6H_5SbO_2)_3OHNa$ 75.35% and $C_6H_5SbO_3HNa$ 24.65%

If, instead of using ¼-⅓ of a molecular equivalent of sodium hydroxide, ½ an equivalent is employed, the resulting salt reacts neutral only in dilute solution, and if 1-2 equivalents are added the salt yields alkaline solutions.

2. Secondary Stibinic Acids.

Diphenylstibinic acid: $(C_6H_5)_2SbO_2H$

(a) A solution of 9.3 g. of aniline in 60 cc. of 5N-hydrochloric acid is diazotized, and after the addition of cracked ice, a solution of 21 g. of phenylstibinous oxide in a little acetic acid is added. When the solution is made alkaline, a vigorous reaction takes place; after the evolution of gas ceases, the impurities are removed by filtration. The crude acid, which separates when the reaction mixture is acidified, is redissolved in dilute sodium hydroxide and reprecipitated with sulfuric acid. It may be further purified by isolation of diphenylstibinic chloride from a solution of the acid in hot dilute hydrochloric acid, decomposition of the chloride with excess dilute alkali and precipitation with acetic acid.[42]

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[39] Ger. Pat. 296,940.

[40a] Ref. 4b; and 27b, p. 353.

[b] Ger. Pat. 267,083.

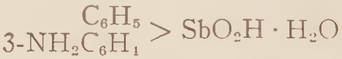
[41] Fargher and Gray: *J. Pharm. and Exper. Therap.*, 18 (1921), 354.

(b) Diphenylstibinous chloride is converted, by the direct addition of chlorine, into the stibinic chloride, which is then hydrolyzed with alkali.[43]

(c) Oxidation of a hot alkaline solution of triphenylstibine with hydrogen peroxide.[44]

Diphenylstibinic acid is a slightly colored powder which melts at *ca.* 285°. Insoluble in water and concentrated hydrochloric acid; soluble in hot, dilute hydrochloric acid. The behavior toward alkali depends upon the method of isolation; the product secured by the method of purification given in (a) is insoluble in dilute alkalies. If, however, the alkaline solution obtained by hydrolysis of the chloride is made slightly acid to phenolphthalein with sulfuric acid, it becomes alkaline again upon standing. By alternate acidification to phenolphthalein and standing, a diphenylstibinic acid separates which is soluble not only in caustic soda but also in aqueous ammonia and sodium carbonate.

3-Amino-diphenylstibinic acid:



$$\begin{matrix} C_6H_5 \\ 3\text{-}NH_2C_6H_4 \end{matrix} > SbO_2H \cdot H_2O$$

A solution of 9.3 g. of aniline in 60 cc. of 5N-hydrochloric acid is diazotized and treated successively with a neutralized solution of 3-aminophenylstibinous chloride hydrochloride and a solution of sodium hydroxide. After the vigorous reaction is over, the solution is filtered and treated with hydrochloric acid; a precipitate forms which redissolves, but when excess acid has been added, the chloride of the stibinic acid precipitates. The latter is collected, washed with 5N-hydrochloric acid and dried. After the red dyestuff has been washed out of the chloride with ether, the material is redissolved in dilute caustic soda. When made slightly acid with hydrochloric acid, the chloride remains in solution, and the filtered acid solution yields a precipitate of the stibinic acid when treated with sodium acetate.[45]

[42] Ref. 1, p. 235.
[43a] Michaelis and Reese: *Ann.*, 233 (1886), 59.
[b] Michaelis and Günther: *Ber.*, 44 (1911), 2319.
[c] Ref. 6b.
[44] Ref. 17a, p. 141.
[45a] Ref. 1, p. 238.
[b] Ger. Pat. 269,205.

m-Amino-diphenylstibinic acid is a pink powder which sinters at *ca.* 200°. Soluble in alkalies, dilute hydrochloric acid, alcohol, and chloroform. Insoluble in ether and benzene.

3,3′-Diamino-diphenylstibinic acid:

$(3\text{-}NH_2C_6H_4)_2SbO_2H \cdot \frac{1}{2}H_2O$

After oxidation of an ammoniacal suspension of 3,3′-diamino-diphenylstibinous oxide with a slight excess of hydrogen peroxide, the crude stibinic acid is precipitated with acetic acid and converted into the hydrochloride of the amino stibinic chloride by treatment with excess hydrochloric acid. An aqueous solution of the chloride yields a precipitate of the free acid when treated with sodium acetate.[46]

Diamino-diphenylstibinic acid is a gray powder which decomposes at *ca.* 230°. Slightly soluble in alcohol; soluble in warm methyl alcohol or acetic acid. The dry substance is not readily soluble in alkalies, but alkaline solutions may be obtained by pouring an aqueous solution of the chloride into caustic soda or ammonia solutions.

4,4′-Diacetylamino-diphenylstibinic acid:

$(4\text{-}CH_3CONHC_6H_4)_2SbO_2H \cdot 3H_2O$

(a) A cold solution of 14 g. of p,p′-diacetylamino-diphenylstibinous oxide in 120 cc. of methyl alcohol is oxidized with 50 cc. of a 3% solution of hydrogen peroxide. The stibinic acid separates at once.[47]

(b) Two grams of tri-p-acetylamino-triphenylstibine is added to a mixture of 6 cc. of 2N-sodium hydroxide, 6 cc. of 3% hydrogen peroxide solution, and 30 cc. of methyl alcohol. After the stibine has dissolved, the filtered solution yields the diacetylamino-diphenylstibinic acid when treated with carbon dioxide.[48]

This stibinic acid is a colorless powder which sinters at about 230° and which dissolves slowly in dilute caustic soda. Such a solution yields precipitates with dilute sulfuric and nitric acids, which redissolve in the presence of excess acid. Hydrochloric acid precipitates the stibinic chloride from all solutions. The acetate crystallizes when a solution of the stibinic acid in hot glacial acetic acid is cooled.

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[46] Ref. 1, p. 241.
[47] Ref. 17a, p. 138.
[48] Ref. 17a, p. 139.

3,3′-Dinitro-diphenylstibinic acid: $(3\text{-}NO_2C_6H_4)_2SbO_2H$

Diphenylstibinic basic nitrate is added to a mixture of nitric and sulfuric acids at 40°; after a short while, the temperature is raised to 55°; the solution is cooled and diluted with ice water. The crude product is reprecipitated from a sodium hydroxide solution with acetic or hydrochloric acid. It may be recrystallized from glacial acetic acid.[49]

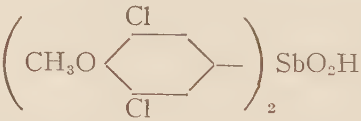
Needles; decomposes indefinitely at about 212°; insoluble in water, alcohol or benzene; its alkali salts dissolve in water to form orange-yellow solutions; the other metallic salts, obtained by double decomposition, are sparingly soluble. When heated in a sealed tube at 130-160° with phosphorus pentabromide and bromine, m-bromonitrobenzene is obtained.

2,2′-Dichloro-diphenylstibinic acid: $(2\text{-}ClC_6H_4)_2SbO_2H \cdot 3H_2O$

Macallum[50] obtained this secondary stibinic acid as the main product of the reaction between antimony oxide and o-chlorodiazobenzene chloride. The crude acid was converted into the stibinic chloride, m.p. 105-110°, and the latter was hydrolyzed again by precipitating an alcoholic solution of it with water. The product was sparingly soluble in alkalies.

This is the first instance in which a secondary stibinic acid is obtained directly from a diazonium compound and antimony trioxide; no previous mention has been made that such substances are formed as by-products. Macallum does not give any details regarding his experimental conditions. This reaction should be studied with respect to other stibinic acids.

3,3′,5,5′-Tetrachloro-4,4′-dimethoxy-diphenylstibinic acid:



$$\left(CH_3O\overset{Cl}{\underset{Cl}{\langle\quad\rangle}}-\right)_2SbO_2H$$

Prepared by hydrolysis of the corresponding stibinic chloride.[51] White amorphous powder; melts with decomposition at 228-229°. Insoluble in ordinary solvents; dissolves gradually in warm dilute sodium hydroxide. Reconverted into the chloride by alcoholic hydrochloric acid.

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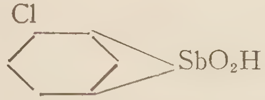
[49] Ref. 6b, p. 2294.

[50] Macallum: *J. Soc. Chem. Ind.*, 42 (1923), 468T.

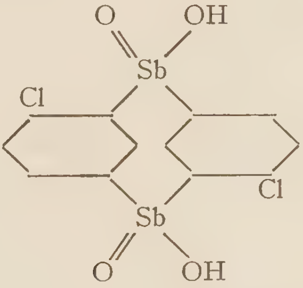
[51] Löloff: *Ber.*, 30 (1897), 2840.

Chloro-m-phenylenestibinic acid:

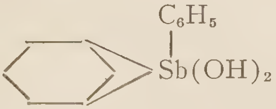


A solution of 32 g. of 3-amino-4-chlorophenylstibinous chloride in 133 g. of hydrochloric acid (sp. gr. 1.084) and 400 cc. of water is diazotized with 7.3 g. of sodium nitrite; the diazonium compound precipitates. After the addition of cracked ice, 250 g. of sodium hydroxide solution (sp. gr. 1.19) is added; nitrogen is evolved vigorously. The filtrate from the insoluble matter yields the crude acid when acidified with hydrochloric acid. After drying, the product is dissolved in warm alcoholic hydrochloric acid and reprecipitated from the filtered and cooled solution with water. It is then reprecipitated from alkaline solution with acid.[52]

Brown powder; decomposes without melting when heated; insoluble in the ordinary solvents; soluble in alkali. Morgan[53] suggests the following formula:



Phenyl-m-phenylenestibinic acid:



3-Aminodiphenylstibinous oxide is diazotized and treated with alkali. The crude product, which is obtained by acidification of the reaction mixture, is dissolved in warm alcoholic hydrochloric acid, reprecipitated with water, dissolved in ether and extracted from the ethereal solution with dilute aqueous sodium hydroxide. Ammonium chloride precipitates the stibinic acid from the alkaline extract.[52]

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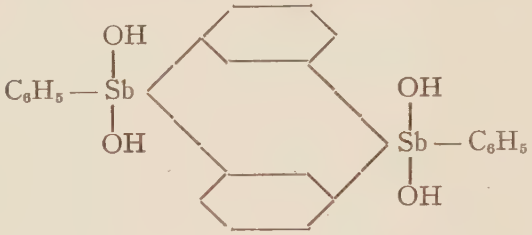
[52] Ger. Pat. 269,205.

[53] Morgan: "Organic Compounds of Arsenic and Antimony," Longmans (1918), p. 321.

Light brown powder; decomposes without melting when heated; readily soluble in warm glacial acetic acid; sparingly soluble in alkalies. Morgan[53] suggests the following formula:



B. Primary Stibinic Chlorides.

Phenylstibinic chloride: $C_6H_5SbCl_4$

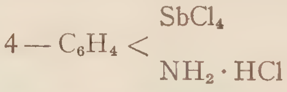
(a) A cold, ethereal solution of phenylstibinous chloride is saturated with chlorine and then evaporated.[54]

(b) When a solution of phenylstibinic acid in concentrated hydrochloric acid is evaporated, the chloride is obtained as an oil which gradually solidifies in a desiccator.[55]

Very hygroscopic crystals; m.p. 60-65°; readily soluble in hydrochloric acid, ether and hot chloroform and benzene; hydrolyzed to the stibinic acid by water. Decomposes gradually in a desiccator—rapidly if heated—forming diphenylstibinic chloride and antimony trichloride.

The hydrochloric acid solution yields precipitates of double salts when treated with amine hydrochlorides. *Ammonium phenyl chlorantimonate:*[56] $(C_6H_5SbCl_5)NH_4$; does not melt even at 260°; readily hydrolyzed by water to form phenylstibinic acid.

4-Aminophenylstibinic chloride hydrochloride:



$$4 - C_6H_4 < \begin{matrix} SbCl_4 \\ NH_2 \cdot HCl \end{matrix}$$

A paste of p-aminophenylstibinic acid is treated with concentrated hydrochloric acid;[57] the chloride is insoluble in concentrated acid. Slightly colored powder; m.p. 155°; readily soluble in methyl alcohol and water. When an acidified, aqueous solution of the chloride is heated, part of the antimony is eliminated.

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[54] Ref. 6c, p. 2913.

[55] Ref. 1, p. 199.

[56] Ref. 1, p. 201.

[57] Ref. 17a, p. 146.

2-Nitrophenylstibinic chloride:

An excess of concentrated hydrochloric acid precipitates this chloride as an oil from a solution of the stibinic acid in methyl alcohol which contains a small quantity of concentrated hydrochloric acid. Upon standing, the oil changes to a crystalline mass which melts indefinitely at about 127° and which is readily soluble in alcohol and ether. The addition of water to the alcohol solution reprecipitates the stibinic acid.[58]

3-Nitrophenylstibinic chloride: $3\text{-}NO_2C_6H_4SbCl_4 \cdot H_2O$

A hot solution of 3-nitrophenylstibinic acid in concentrated hydrochloric acid yields a thick, crystalline paste of the chloride when cooled.[59] After drying *in vacuo* to constant weight, the 3-nitrophenylstibinic chloride melts at 140°, is sparingly soluble in alcohol and ether, and hydrolyzes in water to form the stibinic acid. From a solution of the chloride in hydrochloric acid, ammonium chloride precipitates a crystalline double salt, $(3\text{-}NO_2C_6H_4SbCl_5)NH_4 \cdot \frac{1}{3}H_2O$, which sinters at 235°.

4-Chlorophenylstibinic chloride:

When cooled, a solution of 4-chlorophenylstibinic acid in concentrated hydrochloric acid deposits yellow crystals which, when dried *in vacuo,* lose their yellow color.[60] The chloride deliquesces in the air. A stable, yellow double salt is obtained by adding ammonium chloride to the original hydrochloric acid solution, $(4\text{-}ClC_6H_4SbCl_5)NH_4 \cdot \frac{1}{3}H_2O$. This substance does not melt at 250°, is soluble in methyl alcohol and hydrolyzes in water.

4-Arsonophenylstibinic chloride:

This substance can be isolated as a double salt with pyridine hydrochloride by dissolving the stibinic acid in concentrated hydrochloric acid and adding a solution of pyridine in the same solvent. Colorless, voluminous substance, m.p. 155°. $(H_2O_3AsC_6H_4SbCl_4)_2 \cdot (C_5H_5N \cdot HCl)_3 1\frac{1}{3}H_2O$.[61] An analogous compound can be obtained by using ammonium chloride.

3-Nitro-4-Chlorophenylstibinic chloride:

$3\text{-}NO_2\text{-}4\text{-}ClC_6H_3SbCl_4 \cdot 5H_2O$

The addition of 25 cc. of hydrochloric acid (S.G. 1.19) to a solution of 7 g. of 3-nitro-4-chlorophenylstibinic acid in 30 cc. of hydrochloric acid (sp. gr. 1.126) precipitates the stibinic chloride as colorless crystals[62] which, when air dried, contain 5 molecules of water of crystallization and melt at 80°. Four of the molecules of water may be removed readily by drying *in vacuo;* the resulting monohydrate sinters at 122°. The pentahydrate is somewhat soluble in ether, soluble in warm chloroform, and insoluble in benzol. The double salt from the chloride and ammonium chloride differs from the salts of the other stibinic chlorides. It separates as a colorless precipitate which after air drying is represented by $(C_6H_3NO_2 \cdot Cl \cdot SbCl_4)_2NH_3 \cdot 8H_2O$ and which is soluble in methyl and ethyl alcohols and ether; the other double salts are insoluble in ether. It is decomposed by water.

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[58] Ref. 1, p. 206.
[59] Ref. 1, p. 204.
[60] Ref. 1, p. 208.
[61] Ref. 37, p. 1146.

C. Secondary Stibinic Chlorides.

Diphenylstibinic chloride: $(C_6H_5)_2SbCl_3 \cdot H_2O$

(a) Obtained in crystalline condition by cooling a solution of diphenylstibinic acid in hot dilute hydrochloric acid.[63]

(b) Dry chlorine is passed into diphenylstibinous chloride, and the crude product is recrystallized from dilute hydrochloric acid.[64]

(c) Secured as a by-product in the preparation of triphenylstibine from chlorobenzene and antimony trichloride by the sodium method.[65] By modifying this process, diphenylstibinic chloride may be obtained in yields of 11-16% of the weight of the antimony trichloride.[66] A solution of 48 g. of antimony trichloride and 48 g. of chlorobenzene in 150-200 cc. of dry benzene is added to 20 g. of sodium which has been granulated by melting and shaking under boiling petroleum; it is occasionally necessary to warm the mixture to start the reaction. After 24 hours, the filtered solution is evaporated, and the oily residue is solidified by trituration with alcoholic hydrochloric acid and then dissolved in a small quantity of boiling alcohol. Upon cooling the major part of the triphenylstibinic chloride crystallizes, and the mother liquor, when evaporated, yields a crude diphenylstibinic chloride. The latter is purified by solution in hot dilute hydrochloric acid; the filtered solution deposits the product as colorless crystals.

[62] Ref. 1, p. 210.
[63] Ref. 1, p. 236.
[64] Ref. 43b, p. 2319.
[65] Ref. 43a, p. 58.
[66] Ref. 6b, p. 2293.

(d) By-product in the preparation of triphenylstibinic chloride from mercury diphenyl and antimony trichloride.[67]

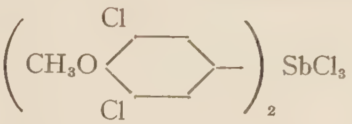
Long needles; m.p. 175-176°, 180°; insoluble in water; soluble in dilute hydrochloric acid, and alcohol. When treated in alcoholic solution with silver nitrate, a diphenylstibinic nitrate is formed which is partially hydrolyzed during isolation; a basic nitrate, colorless needles decomposing at 206°, is obtained.

3,3′-Diamino-diphenylstibinic chloride dihydrochloride:

$(3\text{-ClH} \cdot NH_2C_6H_4)_2SbCl_3 \cdot 2H_2O$

Prepared from 3,3′-diaminodiphenylstibinic acid by the action of excess hydrochloric acid.[68] Fine crystals; do not melt even at 250°; soluble in water; hydrolyzed to the stibinic acid by aqueous sodium acetate.

3,3′,5,5′-Tetrachloro-4,4′-dimethoxy-diphenylstibinic chloride:



Formed by the action of chlorine on tri-p-anisylstibine in chloroform solution. The residue obtained by evaporation of the chloroform is dissolved in benzene; the product separates gradually in a crystalline condition. Moisture must be excluded during the entire experiment.[69] Colorless crystals; m.p. 184°; readily soluble in chloroform and ether; difficultly soluble in benzene and absolute alcohol; insoluble in petroleum ether. Hydrolyzed by water.

D. Tertiary Stibinic Oxides and Salts.

Trimethylstibinic oxide: $(CH_3)_3SbO$

An aqueous solution of trimethylstibinic sulfate is treated with barium hydroxide, filtered, and evaporated. The residue is dissolved in alcohol, and the solution is evaporated in the absence of carbon dioxide.[70]

White crystalline mass; very soluble in water and alcohol, but insoluble in ether.

Trimethylstibinic salts: Chloride: $(CH_3)_3SbCl_2$

Separates as a white crystalline solid when a carbon bisulfide solution of the stibine is treated with chlorine or an aqueous solution of the stibinic oxide is treated with hydrochloric acid.[71]

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[67] Ref. 6c, p. 2911.
[68] Ref. 1, p. 241.
[69] Ref. 51, p. 2839.
[70] Landolt: *J. prakt. Chem.*, [1] **84** (1861), 331.

Colorless needles; soluble in hot water but insoluble in cold water.

Bromide: $(CH_3)_3SbBr_2$. Separates as a white crystalline solid when bromine is added to a cold, alcoholic solution of the stibine.[72] Soluble in hot alcohol and hot water but difficultly soluble in the cold.

Iodide: $(CH_3)_3SbI_2$. (a) Separates in fine, white needles when the stibine is treated with iodine in the presence of alcohol.[72]

(b) Coarse metallic antimony is heated at 140° in a sealed tube with methyl iodide.[73]

Soluble in hot alcohol and water. The crystals gradually become yellow in the air.

Oxyhalides: $[(CH_3)_3SbX]_2O$. An aqueous solution of the stibinic halide is halved, and one portion is treated with silver oxide, filtered and added to the other portion of the original solution. When this solution is evaporated the oxyhalide is obtained in a crystalline condition.[74] The chloride and bromide are colorless, but the iodide is yellow.

Sulfate: $(CH_3)_3SbSO_4$. A hot, aqueous solution of the stibinic iodide is treated with silver sulfate, filtered and evaporated. The residue is a white, semi-resinous mass which is soluble in water but only slightly soluble in alcohol.[75]

Sulfide: $(CH_3)_3SbS$. An ethereal solution of the stibine is warmed with sulfur, filtered and evaporated; or an aqueous solution of the stibinic oxide is treated with hydrogen sulfide and evaporated.[76] Small, scaly crystals; soluble in alcohol or ether but difficultly soluble in cold water.

Nitrate: $(CH_3)_3Sb(NO_3)_2$. The stibine dissolves in nitric acid with the evolution of heat and oxides of nitrogen; when the solution is cooled, colorless crystals of the nitrate are obtained. The same product is secured by treating a warm solution of the stibinic iodide with silver nitrate and evaporating the filtrate from the silver iodide.[77]

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[71] Ref. 70, p. 334.
[72] Ref. 70, p. 335.
[73] Buckton: *Quart. J. Chem. Soc.*, **13** (1861), 119.
[74a] Friedländer: *J. prakt. Chem.*, [1] **70** (1857), 336.
[b] Hantzsch and Hibbert: *Ber.*, **40** (1907), 1512.
[75] Ref. 70, p. 338.
[76] Ref. 70, p. 333.

Thiocyanate. An alcoholic solution of the stibinic chloride is heated with potassium thiocyanate, filtered and cooled. The thiocyanate separates in white crystals which are readily soluble in hot water but insoluble in cold water.[78]

Triethylstibinic oxide: $(C_2H_5)_3SbO$

(a) An alcoholic solution of the stibine is shaken with mercuric oxide, and the filtrate from the mercury is evaporated.[79]

(b) An aqueous solution of the stibinic sulfate is treated with barium hydroxide, and the filtrate from the barium sulfate is evaporated on a water bath. The residue, dissolved in alcohol, is treated with carbon dioxide, and the filtrate from the barium carbonate is evaporated.

Colorless, viscous mass which does not crystallize; soluble in water and alcohol but only slightly soluble in ether. Reacts with acids to form salts and precipitates metallic hydroxides from solutions of their salts.

Tri-ethylstibinic Salts:

Chloride: $(C_2H_5)_3SbCl_2$. A concentrated solution of the stibinic nitrate is treated with concentrated hydrochloric acid; the chloride precipitates as a colorless oil which is purified by precipitation from alcoholic solution with water. Or, triethylstibine may be treated with concentrated hydrochloric acid.[80]

Colorless liquid; sp. gr. 1.540 at 17°; does not solidify even at — 17°; cannot be distilled without decomposition; insoluble in water; soluble in alcohol and ether; decomposed by concentrated sulfuric acid with the liberation of hydrochloric acid.

Bromide: $(C_2H_5)_3SbBr_2$. A cold alcoholic solution of the stibine is treated with a similar solution of bromine; the addition of water precipitates the product as a clear, colorless oil which is washed with water and reprecipitated from alcoholic solution with water.[81]

Colorless liquid; sp. gr. 1.953 at 17°; solidifies to white crystals at — 10°; insoluble in water but soluble in alcohol, and ether; cannot be distilled without decomposition; yields hydrobromic acid when treated with concentrated sulfuric acid and bromine when treated with chlorine. Its vapors are very irritating to the eyes and nose.

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[77] Ref. 70, p. 337.
[78] Ref. 74b, p. 1513.
[79] Löwig and Schweizer: *Ann.*, **75** (1850), 330.
[80] Ref. 79, p. 342.
[81] Ref. 79, p. 340.

Iodide: $(C_2H_5)_3SbI_2$. (a) A cold, alcoholic solution of the stibine is treated with iodine as long as the latter is reduced; the solution yields colorless crystals when evaporated. The crude product is recrystallized from alcohol and ether.[82]

(b) Coarse metallic antimony is heated at 140° in a sealed tube with ethyl iodide.[83]

Colorless needles; m.p. 70.5°; soluble in water, alcohol and ether. Reacts with hydrochloric acid and sulfuric acid with the liberation of hydrogen iodide and yields iodine when treated with chlorine or bromine.

Sulfide: $(C_2H_5)_3SbS$. (a) The stibine and sulfur combine exothermically under water; the aqueous solution is decanted and evaporated to crystallization.[84]

(b) An ethereal solution of the stibine is boiled with sulfur, filtered while hot and cooled, the sulfide crystallizes readily. The crude material is exposed to the air in order that any unchanged stibine may oxidize and is then recrystallized from ether.[84]

(c) An alcoholic solution of the stibinic oxide is treated with hydrogen sulfide and evaporated to crystallization.[85]

Colorless crystals; m.p. 100°; stable in the air; soluble in water, alcohol, and warm ether; insoluble in cold ether. Aqueous solutions yield hydrogen sulfide when acidified, and metallic sulfides when treated with metallic salts. When treated in aqueous solution with mercuric cyanide the filtrate from the mercuric sulfide contains the stibinic cyanide but the latter is quite unstable.[86]

Selenide. An ethereal solution of the stibine is boiled with precipitated selenium; the solution deposits crystals of the selenide when cooled, but the compound is unstable in the air.[87]

Nitrate: $(C_2H_5)_3Sb(NO_3)_2$. (a) Either the stibine or the stibinic oxide is dissolved in dilute nitric acid; the former dissolves with the evolution of heat and nitrous fumes. After filtration, the solution is evaporated to crystallization. An aqueous solution of the crude product is again evaporated.[88]

[82] Ref. 79, p. 338.
[83] Ref. 73, p. 116.
[84] Ref. 79, p. 335.
[85] Merck: *Ann.*, **97** (1856), 333.
[86] Ref. 79, p. 344.
[87] Ref. 79, p. 337.
[88] Ref. 79, p. 332.

(b) Triethylstibinic iodide is treated in aqueous solution with silver nitrate, and the filtrate from the silver iodide is evaporated to crystallization.[89]

Large, rhombic crystals; m.p. 62.5°; soluble in water; difficultly soluble in alcohol, and insoluble in ether.

Sulfate: $(C_2H_5)_3SbSO_4$. (a) Aqueous solutions of the stibinic sulfide and copper sulfate are mixed, and the filtrate from the copper sulfide is evaporated. The sirup crystallizes quite slowly.[90]

(b) An aqueous solution of the stibinic iodide is shaken with silver sulfate, and the filtrate from the silver iodide is evaporated to a sirup.[89]

Colorless crystals; very soluble in water; fairly soluble in alcohol; insoluble in ether. Reacts with concentrated hydrochloric acid forming a precipitate of the stibinic chloride.

Triamylstibinic oxide: $(C_5H_{11})_3SbO$. Obtained as a resinous mass by spontaneous evaporation of an ether solution of the stibine in the air. Insoluble in water but soluble in alcohol.[91]

Triamylstibinic salts: $(C_5H_{11})_3SbX_2$. *Bromide* obtained as an oil by adding an alcoholic solution of bromine to a solution of the stibine in a mixture of alcohol and ether and precipitating the product with water.[92]

Chloride: separates as a viscous oil when an alcoholic solution of the oxide is treated successively with hydrochloric acid and water.[91]

Iodide prepared either by treating the stibine with iodine or the oxide with hydriodic acid; the product is precipitated from alcohol solution by the addition of water.[93]

Nitrate. An alcoholic solution of the stibinic iodide is treated with silver nitrate. The filtrate from the silver iodide gradually separates into 2 layers; the yellow, upper layer yields white crystals of the nitrate when evaporated. The red, lower layer deposits an additional quantity of the crystalline nitrate when diluted with a mixture of water and alcohol.[93]

Sulfate. An alcoholic solution of the iodide is treated with silver sulfate; the filtrate, when evaporated, yields the sulfate as an oil.

Phenyl-dimethylstibinic halides. Chloride: $C_6H_5(CH_3)_2SbCl_2$.

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[89] Ref. 85, p. 333.
[90] Ref. 79, 334.
[91] Berlé: *Ann.,* 97 (1856), 318.
[92] Ref. 91, p. 317.
[93] Ref. 91, p. 319.

The tertiary stibine, dissolved in carbon tetrachloride, is treated with chlorine, and the solvent is removed by evaporation.[94] Yield—quantitative. Long, colorless prisms, m.p. 128°, readily soluble in benzene and carbon tetrachloride.

Bromide: $C_6H_5(CH_3)_2SbBr_2$. Prepared by method used for chloride.[94] Colorless plates, m.p. 112-113°.

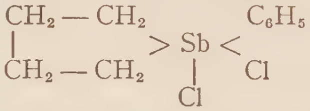
Iodide: $C_6H_5(CH_3)_2SbI_2$. Precipitates when a petroleum ether solution of iodine is added to a similar solution of the stibine.[94] Crystalline powder, m.p. 98.5-99°. If an excess of iodine is used dark colored products are formed.

Phenyl-diethylstibinic chloride:[95] $C_6H_5(C_2H_5)_2SbCl_2$. Colorless oil, decomposes upon distillation; *bromide*—colorless oil, decomposes upon distillation; *iodide*—pale yellow, hexagonal plates; m.p. 88.5-89°.

Methyl-diphenylstibinic chloride and bromide: $CH_3(C_6H_5)_2SbX_2$. The tertiary stibine and the halogen are combined in carbon tetrachloride solution.[96] *Chloride:* colorless prisms, m.p. 144°. *Bromide:* colorless prisms, m.p. 148°.

Ethyl-diphenylstibinic halides are formed when the tertiary stibine, dissolved in carbon tetrachloride, is treated with chlorine or bromine.[97] *Chloride:* colorless plates, m.p. 163-164°; *bromide:* plates, m.p. 158°.

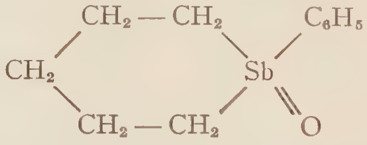
Cyclotetramethylene-phenylstibinic chloride:



Dry chlorine is passed into a carbon tetrachloride solution of the stibine and the solvent is then removed by evaporation.[98] Colorless crystals; m.p. 150°.

Bromide. Prepared in the same manner as the chloride; colorless needles; m.p. 149°.

Cyclopentamethylene-phenylstibinic oxide:



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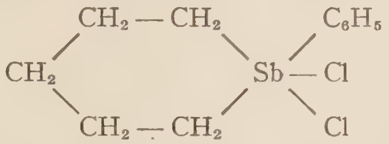
[94] Grüttner and Wiernik: *Ber.,* 48 (1915), 1760.
[95] Ref. 94, p. 1761.
[96] Ref. 94, p. 1763.
[97] Ref. 94, p. 1764.
[98] Grüttner and Krause: *Ber.,* 49 (1916), 443.

From the stibine by atmospheric oxidation at room temperature.[99] Colorless powder, does not melt even at 280°. Soluble in alcohol but insoluble in petroleum ether.

Cyclopentamethylene-phenylstibinic chloride:



From the stibine and chlorine in carbon tetrachloride solution.[100] White, crystalline powder; m.p. 141-2°.

Triphenylstibinic hydroxide: $(C_6H_5)_3Sb(OH)_2$. (a) Triphenylstibinic bromide is added to warm alcoholic potassium hydroxide, and the mixture is boiled till the reaction is complete. The filtrate from the potassium bromide is treated with carbon dioxide to remove the excess potassium hydroxide. The residue obtained by evaporating the filtrate from the potassium carbonate is washed with ether and precipitated from acetic acid solution by the addition of water.[101]

(b) Triphenylstibine is oxidized in cold, aqueous suspension with sodium peroxide or in the presence of cold, aqueous caustic potash with hydrogen peroxide.[102]

White, crystalline powder; m.p. 212°; insoluble in ether or petroleum; soluble in alcohol and glacial acetic acid.

Triphenylstibinic Salts:

Chloride: $(C_6H_5)_3SbCl_2$. (a) Mercury diphenyl, antimony trichloride and dry xylene are heated in a sealed tube at 130° for a long time.[103]

(b) Separates when chlorine is passed into a cold ligroin or petroleum ether solution of triphenylstibine.[104]

(c) A by-product in the preparation of triphenylstibine by the Fittig reaction.[104b]

Long, colorless needles; m.p. 141.5°, 143°; difficultly soluble in ether or alcohol; readily soluble in benzene, carbon bisulfide and

[99] Grüttner and Wiernik: *Ber.,* 48 (1915), 1484.
[100] Ref. 99, p. 1485.
[101] Ref. 43a, p. 51.
[102] Ger. Pat. 360,973.
[103] Ref. 6c, p. 2910.
[104a] Pfeiffer: *Ber.,* 37 (1904), 4621.
[b] Ref. 43a, p. 49.

hot alcohol; not hydrolyzed very easily by water, but alcoholic alkali converts it readily into the dihydroxide.

Bromide. Separates as a white, crystalline powder when bromine is added dropwise to a solution of triphenylstibine in glacial acetic acid; it is recrystallized from benzene.[105] Needles; m.p. 216°; difficultly soluble in petroleum ether, alcohol, ether and cold acetic acid; soluble in benzene, carbon bisulfide, and hot acetic acid.

Iodide. Precipitates when solutions of the stibine and iodine in petroleum ether are mixed; obtained as white plates, m.p. 153°, by recrystallization from a mixture of benzene and petroleum ether.[106] Soluble in benzene, but not in ether, alcohol, or petroleum ether.

Hydroxy-chloride: $(C_6H_5)_3Sb(OH)Cl$. An alcoholic solution of the stibinic chloride is added to boiling water and evaporated to crystallization;[107] transparent, colorless spicules; m.p. 218°.

Sulfide: $(C_6H_5)_3SbS$. Hydrogen sulfide is introduced into a filtered solution of triphenylstibinic bromide (10 g.) in 160 cc. saturated alcoholic ammonia with constant agitation till a very faint yellow color appears. The stream of hydrogen sulfide is discontinued, and as soon as the yellow tinge has disappeared, the crystals are collected on a filter and washed with alcohol.[108] Yield 80%.

Colorless crystals; m.p. 119-120°; readily soluble in benzene, chloroform, and acetic acid; difficultly soluble in alcohol, ether, and petroleum ether. Prolonged heating or dilute acids decompose it into triphenylstibine and sulfur; refluxing in a mixture of alcohol and benzene with iron or copper powder yields triphenylstibine.[109]

Sulfate: $(C_6H_5)_3SbSO_4$. Separates in small, white crystals when triphenylstibine is warmed with concentrated sulfuric acid.[110] Melts above 300°; soluble in concentrated sulfuric acid; sparingly soluble in alcohol; insoluble in water; decomposed by warm aqueous sodium hydroxide forming triphenylstibinic hydroxide.

Hydroxy-sulfate: $[(C_6H_5)_3Sb(OH)]_2SO_4$. An alcoholic solution of the stibinic chloride is added to a boiling aqueous solution of silver sulfate; the product is isolated from the filtrate from the silver chloride by evaporation.[111] Colorless, nodular crystals; melts at 252° with decomposition; insoluble in cold water.

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[105] Ref. 43a, p. 50.
[106] Ref. 43a, p. 51.
[107] Morgan, Micklethwait, and Whitby: *J. Chem. Soc.*, 97 (1910), 37.
[108] Kaufmann: *Ber.*, 41 (1908), 2764; U. S. Pat. 1,060,765; Ger. Pat. 223,694.
[109] Ger. Pat. 240,316.
[110] May: *J. Chem. Soc.*, 97 (1910), 1958.

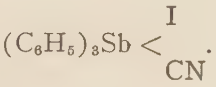
Acetate: $(C_6H_5)_3Sb(OCOCH_3)_2$. Crystallizes when a solution of triphenylstibinic oxide in hot glacial acetic is cooled.[112] M.p. 215°. Readily soluble in hot methyl alcohol; converted into the stibinic chloride by hydrochloric acid.

Nitrate: $(C_6H_5)_3Sb(NO_3)_2$. Deposits in a crystalline condition when a solution of the hydroxide in nitric acid or the stibine in fuming nitric acid is cooled.[113] Plates; m.p. 156°; insoluble in water; soluble in hot concentrated nitric acid or alcohol.

Hydroxy-nitrate: $(C_6H_5)_3Sb(OH)(NO_3)$. (a) Triphenylstibinic chloride reacts with silver nitrate in warm alcoholic solution to form the stibinic nitrate which, during isolation, undergoes partial hydrolysis. By dissolving this material in boiling water, it is hydrolyzed to the hydroxy nitrate which crystallizes when the solution is cooled.[114]

(b) Triphenylstibine is added to a 30% solution of fuming nitric acid in glacial acetic acid; the hydroxy nitrate separates after dilution with water.[115]

Colorless leaflets; soften at 220° and melt at 224-225°; insoluble in cold water; very soluble in alcohol; reduced by Devarda's alloy (Al-Cu couple) to triphenylstibine.

Iodo-cyanide:  $(C_6H_5)_3Sb<\begin{matrix}I\\CN\end{matrix}$. A colorless or pale yellow solid (m.p. 174°) obtained by treating a cold, dry, ethereal solution of the stibine with cyanogen iodide.[116] It is only fairly stable.

Hydroxy-iodide: $(C_6H_5)_3Sb(OH)I$. If triphenylstibine is treated with cyanogen iodide in ordinary ether, or if the above iodocyanide is recrystallized, the hydroxy-iodide is obtained[117] as white leaflets (m.p. 196°) which are soluble in most organic solvents except ether and light petroleum. If this substance is heated, iodobenzene is evolved; with alcoholic silver nitrate it yields the hydroxy-nitrate.

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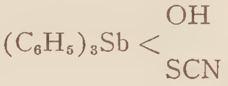
[111] Morgan, Micklethwait, and Whitby: *J. Chem. Soc.*, **97** (1910), 37.
[112] Ref. 17a, p. 142.
[113] Ref. 43a, p. 52.
[114] Ref. 107, p. 36.
[115] Ref. 6b, p. 2286.
[116] Ref. 74b, p. 1514.
[117] Wilkinson and Challenger: *J. Chem. Soc.*, **125** (1924), 860.

Thiocyanate: $(C_6H_5)_3Sb(SCN)_2$. The stibine is treated with a dry, ethereal solution of thiocyanogen prepared by treating lead thiocyanate with bromine, and the product is precipitated by adding light petroleum. White crystals, m.p. 105-6°, soluble in organic solvents except light petroleum.[117a]



Hydroxy-thiocyanate: $(C_6H_5)_3Sb<\begin{matrix}OH\\SCN\end{matrix}$. Prepared by boiling the thiocyanate with water; forms as a by-product when the stibinic chloride is treated with lead thiocyanate.[117a] White, crystalline solid, melting at 227-8°.

Tri-sulfo-triphenylstibinic hydroxide: $(HO_3SC_6H_4)_3Sb(OH)_2 \cdot 3H_2O$. Triphenylstibinic hydroxy-sulfate is sulfonated at 100° with fuming sulfuric acid.[118] A brittle, yellow mass; the yield is about 40% of the weight of the hydroxysulfate. The nature of this substance has not been studied very extensively.

Tri-3-nitro-triphenylstibinic hydroxide: $(3\text{-}NO_2C_6H_4)_3Sb(OH)_2$. (a) Triphenylstibine is added slowly to an excess of a mixture of sulfuric and nitric acids (3:1) at 40°; the reaction mixture is diluted at a temperature below 25°.[119]

(b) Triphenylstibinic hydroxy-nitrate (3 g.) is added slowly to a mixture of 25 cc. of nitric acid (sp. gr. 1.5) and 6 cc. of sulfuric acid at 40°, and the temperature is then kept at 55° for 2 hours. After cooling, it is diluted with ice water. The crude product is reprecipitated from sodium hydroxide solution with hydrochloric acid.[120]

Transparent, pale yellow crystals; m.p. 190-191°; may be recrystallized from glacial acetic acid; somewhat soluble in alcohol and ether; insoluble in water, benzene, and light petroleum. When boiled with alcoholic hydrochloric acid a mixture of stibinic chloride and hydroxy-chloride is formed. Yields alkali salts which dissolve in water to form brownish-orange solutions from which salts with various other metals may be obtained by double decomposition. By heating in chloroform solution with phosphorus pentabromide and bromine in a sealed tube at 130-160°, m-bromo-nitrobenzene is obtained in 70% yield.

[117a] Challenger, Smith, and Paton: *J. Chem. Soc.*, **123** (1923), 1052.
[118] Ref. 6b, p. 2286.
[119] Ref. 110, p. 1958.
[120] Ref. 6b, p. 2290.

Tri-3-nitro-triphenylstibinic chloride: $(3\text{-}NO_2C_6H_4)_3SbCl_2$. Triphenylstibinic chloride is nitrated in concentrated sulfuric acid solution; the yield is small.[121]

Small crystals; m.p. 157°; readily soluble in concentrated nitric acid or glacial acetic acid.

Tri-p-anisylstibinic salts.

Chloride: $(4\text{-}CH_3OC_6H_4)_3SbCl_2$. A chloroform solution of the stibine is treated with alcohol and then with alcoholic cupric chloride till cuprous chloride no longer precipitates. The filtrate is evaporated, and the residue is extracted with benzene. After evaporation of the benzene, the dichloride is redissolved in chloroform and precipitated with petroleum ether.[122] Fine white crystals; m.p. 116-117°; readily soluble in benzene, chloroform, ether; difficultly soluble in alcohol; insoluble in petroleum ether. Crystallizes from a benzene solution with one molecule of benzene: $(CH_3OC_6H_4)_3SbCl_2 \cdot C_6H_6$ large prisms; m.p. 82-83° if heated rapidly, 116-117° if heated slowly.

Bromide. A chloroform solution of the stibine is treated with bromine and the product is precipitated with petroleum ether.[122] Thin, colorless plates; m.p. 123°; readily soluble in benzene, ether, chloroform; difficultly soluble in alcohol; insoluble in petroleum ether. Crystallizes from benzene in rhombic prisms; m.p. 81-82°; contains one molecule of benzene. The bromide is reduced to the stibine by excess ammonium sulfide.

Iodide. From the stibine and iodine in chloroform solution; after the addition of absolute alcohol the solvents are removed by evaporation.[123] Yellow leaflets; m.p. 116°. Readily soluble in ether, benzene, chloroform; insoluble in petroleum ether.

Nitrate: $(4\text{-}CH_3OC_6H_4)_3Sb(NO_3)_2$. From the bromide and silver nitrate in alcoholic solution. The filtrate from the silver bromide is evaporated, and the dinitrate is extracted from the residue with benzene; the extract is then evaporated.[123] Small needles; m.p. 217° with decomposition.

Tri-p-anisylstibinic oxide: $(4\text{-}CH_3OC_6H_4)_3SbO$. The halides are decomposed with alkalies.[123] Crystalline; m.p. 191°; very readily soluble in benzene, ether, chloroform; less soluble in alcohol. Reacts with halogen acids forming the stibinic halides.

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[121] Ref. 110, p. 1958.

[122] Ref. 51, p. 2837.

[123] Ref. 51, p. 2838.

Tri-p-phenetylstibinic salts:[124] $(4\text{-}C_2H_5OC_6H_4)_3SbX_2$.

Chloride. From the stibine and cupric chloride in hot alcoholic solution.[125] Crystalline; m.p. 84°; difficultly soluble in petroleum ether.

Bromide. Separates when solutions of the stibine and bromine in petroleum ether are mixed. Fine needles; m.p. 110-111°; readily soluble in benzene, ether, and chloroform; slightly soluble in alcohol; insoluble in petroleum ether. Instead of yielding an oxide when treated with alcoholic sodium hydroxide, the bromide is reconverted into the stibine.

Iodide. From the components in chloroform solution; prismatic crystals; m.p. 121-122°.

Nitrate. From the bromide and silver nitrate in alcoholic solution; crystals, m.p. 151-152°.

Tri-p-tolylstibinic oxide: $(4\text{-}CH_3C_6H_4)_3SbO$. Tri-p-tolylstibinic bromide is warmed with alcoholic potassium hydroxide, and the residue obtained by evaporation of the filtered, alcohol solution is washed with warm water. The crude product is recrystallized from benzene.[126]

Small, white needles; m.p. 223.5°; readily soluble in alcohol and chloroform, but difficultly soluble in ether.

Tri-p-tolylstibinic hydroxide: $(4\text{-}CH_3C_6H_4)_3Sb(OH)_2$. A suspension of tri-p-tolylstibine in cold aqueous potash is oxidized with hydrogen peroxide;[127] m.p. 225°.

Michaelis and Genzken [126a] isolated a crystalline compound melting at 169.5° by adding water to a solution of the stibinic oxide in hot glacial acetic acid until the solution became slightly turbid and then cooling the solution. They considered their substance to be tri-p-tolylstibinic hydroxide. However, Kaufmann [127] found that the stibinic hydroxide melts at 225° and that the acetate derived from it melts at about 165°. It appears, therefore, that the former investigators were probably dealing with the basic acetate; cf. below.

Tri-p-tolylstibinic halides: $(4\text{-}CH_3C_6H_4)_3SbX_2$. Petroleum ether solutions of the tertiary stibine are treated with halogens; the addition products separate directly and may be recrystallized from alcohol-benzene mixtures.[128]

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[124] Ref. 51, p. 2842.

[125] Cf. Tri-p-anisylstibinic chloride.

[126a] Michaelis and Genzken: *Ber.*, 17 (1884), 925

[b] *Ann.*, 242 (1887), p. 174.

[127] Ger. Pat. 360,973.

Chloride. Prisms; m.p. 156.5°. *Bromide.* M.p. 233-234°. *Iodide.* M.p. 182.5°.

The halides are soluble in chloroform and benzene, but insoluble in alcohol, petroleum ether and ether. The iodide yields a basic iodide—$(4\text{-}CH_3C_6H_4)_3Sb(OH)I$, m.p. 218-219°—upon partial hydrolysis. Hydrogen sulfide reduces the halides in alcoholic ammonia to the free stibine.

Tri-p-tolylstibinic basic acetate: $(4\text{-}CH_3C_6H_4)_3Sb(OH)OCOCH_3$. Obtained as colorless crystals by evaporation of a solution of the oxide in glacial acetic acid; m.p. 168-169°; soluble in acetic acid, chloroform and benzene, difficultly soluble in alcohol, ether and petroleum ether.[129] The corresponding formate may be obtained in a similar way; small needles.

Tri-o-tolylstibinic halides: $(2\text{-}CH_3C_6H_4)_3SbX_2$. Precipitate when ethereal solutions of the stibine are treated with halogens; the crude products are recrystallized from mixtures of alcohol and chloroform or ether and benzene.[130]

Chloride. Needles; m.p. 178-179°. *Bromide.* M.p. 209-210°. *Iodide.* Slightly yellow crystals; m.p. 174-175°.

Tri-o-tolylstibinic oxide: $(2\text{-}CH_3C_6H_4)_3SbO$. The stibinic bromide is treated with alcoholic potassium hydroxide.[131] White, amorphous powder; m.p. 220°.

Di-o-tolyl-p-tolylstibinic bromide: $(2\text{-}CH_3C_6H_4)_2(4\text{-}CH_3C_6H_4)SbBr_2$. Colorless crystals prepared from the stibine and bromine;[132] m.p. 185-186°.

Tri-m-tolylstibinic halides: $(3\text{-}CH_3C_6H_4)_3SbX_2$. Prepared by treating the stibine, dissolved in light petroleum, with halogens.[133]

Chloride. Colorless needles; m.p. 137-138°. *Bromide.* Slightly colored crystals; m.p.. 113°. *Iodide.* White crystalline powder; m.p. 138-139°. These compounds are readily soluble in benzene, ether and chloroform, but insoluble in petroleum ether.

Tri-m-tolylstibinic oxide: $(3\text{-}CH_3C_6H_4)_3SbO$. Prepared from the stibinic bromide by the action of alcoholic potassium hydroxide.[134] Yellowish white, amorphous powder; softens at 186°, becomes transparent at 210°; insoluble in water; slightly soluble in alcohol, benzene and chloroform.

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[128] Ref. 126a, p. 925; Ref. 126b, p. 172; Ref. 104a, p. 4622.

[129] Ref. 126b, p. 175.

[130] Ref. 126b, p. 182.

[131] Ref. 126b, p. 183.

[132] Ref. 126b, p. 176.

[133] Ref. 126a, p. 925; Ref. 126b, p. 186.

Tri-m-tolylstibinic basic acetate: $(3\text{-}CH_3C_6H_4)_3Sb(OH)OCOCH_3$.

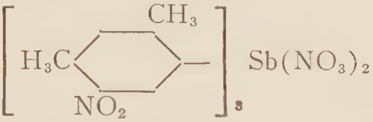
Crystallizes from a solution of the oxide in acetic acid;[134] m.p. 142-143°; soluble in benzene and chloroform but difficultly soluble in ether, alcohol, and petroleum ether.

Tri-m-tolylstibinic sulfide: $(3\text{-}CH_3C_6H_4)_3SbS$. Precipitates when an alcoholic ammonia solution of the stibinic chloride is treated with hydrogen sulfide; the white powder is recrystallized from a mixture of benzene and alcohol.[134] Colorless crystals; m.p. 162-163°; soluble in benzene and chloroform; difficultly soluble in ether, alcohol, and petroleum ether.

Tri-p-xylylstibinic chloride: $[2,5\text{-}(CH_3)_2C_6H_3]_3SbCl_2$. A solution of tri-p-xylylstibine (2.17 g.) in benzene (30 cc.) is treated with 1.55 g. of thallic chloride. After standing overnight the thallous chloride is filtered out, and 1.3 g. of the crude stibinic chloride is obtained by evaporation of the filtrate.[135] M.p. 230-231°; crystalline powder, soluble in cold chloroform, acetone, or benzene; moderately soluble in pyridine; insoluble in light petroleum.

Tri-m-xylylstibinic chloride: $[2,4\text{-}(CH_3)_2C_6H_3]_3SbCl_2$. A cold chloroform solution of tri-m-xylylstibine is saturated with chlorine and spontaneously evaporated.[136] White, granular crystals; m.p. 189°. *Bromide.* Crystalline powder; m.p. 195°; prepared by adding bromine to a chloroform solution of the stibine till the solution is slightly colored.

Tri-5-nitro-tri-m-xylylstibinic nitrate:



Tri-m-xylylstibine (21 g.) is added slowly to nitric acid (100 cc.; sp. gr. 1.16); after heating for 20 minutes on a water bath, the mixture is poured into 3 l. of water. The precipitate (38.2 g.) is a mixture of hydroxy nitrate and nitrate; the latter is obtained by repeated crystallization from alcohol.[137]

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[134] Ref. 126b, p. 187.

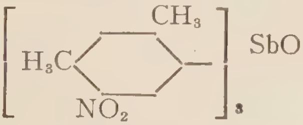
[135] Goddard: *J. Chem. Soc.*, **123** (1923), 1170.

[136] Goddard: *J. Chem. Soc.*, **124** (1923), 2319.

[137] Ref. 136, p. 2320.

White, crystalline powder; sinters at 150°, melts at 175°; soluble in light petroleum, hot chloroform, or acetic acid; slightly soluble in alcohol. When heated in chloroform solution with phosphorus pentabromide at 130° for 5 hours, 4-bromo-6-nitro-m-xylene is formed; 65% yield.

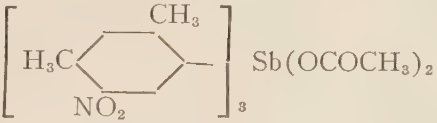
Tri-5-nitro-tri-m-xylylstibinic oxide:



The corresponding stibinic nitrate (5 g.) is boiled in absolute alcoholic solution (300 cc.) containing phosphorous acid (25 g.) for 5 hours and diluted with 2 l. of water.[138] Yield: 3.8 g.

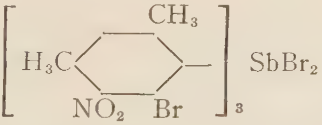
White, crystalline powder; sinters at 210°, melts at 218°; soluble in alcohol; a chloroform solution is orange colored.

Tri-5-nitro-tri-m-xylylstibinic acetate:



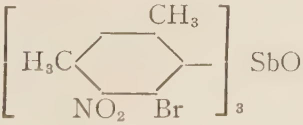
Precipitated from a glacial acetic acid solution of the stibinic oxide by ether.[138] White precipitate; softens at 160°; melts at about 198°.

Tri-6-bromo-tri-5-nitro-tri-m-xylylstibinic bromide:



From the corresponding stibine and bromine in chloroform solution; the product is precipitated with light petroleum and recrystallized from a petroleum-chloroform mixture.[138] White, crystalline powder.

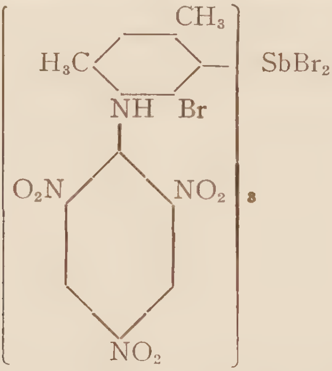
Tri-6-bromo-tri-5-nitro-tri-m-xylylstibinic oxide:



[138] Ref. 136, p. 2322.

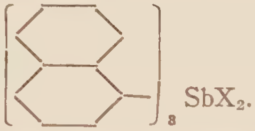
Precipitates when a chloroform solution of the trinitro-trixylylstibinic oxide is treated with a solution of bromine in light petroleum.[138] White crystals; m.p. 162°.

Tripicryl-tri-5-amino-tri-6-bromo-tri-m-xylylstibinic bromide:



The tripicrylaminoxylylstibine (0.5 g.) dissolved in 5 cc. of chloroform is treated with a light petroleum solution of bromine till the orange color changes to red. The product is precipitated by the addition of light petroleum;[139] yield 0.5 g. Lemon-yellow, crystalline powder; m.p. 188°.

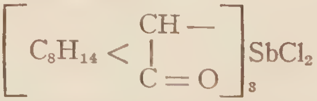
Tri-α-naphthylstibinic halides:



Prepared by adding the stibine to a carbon tetrachloride solution of chlorine or bromine, diluting with light petroleum, and extracting the solid repeatedly with hot chloroform. The residue is the stibinic halide.[140]

Chloride. White, m.p. 260°. *Bromide.* Pale yellow, m.p. 229°.

Tricamphorylstibinic chloride:



$$\left[C_8H_{14} < \begin{matrix} CH- \\ | \\ C=O \end{matrix} \right]_3 SbCl_2$$

A toluene solution of antimony trichloride is added to a suspension of sodium camphor[141] in toluene; after the initial reaction is over the mixture is heated on a water bath and decomposed with water. The mother liquor from the antimony oxide is distilled with steam; the residue, containing the tricamphorylstibinic chloride, is extracted with benzene, and the extract is evaporated to crystallization.[142]

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[139] Ref. 136, p. 2323.

[140] Challenger and Pritchard: *J. Chem. Soc.*, **125** (1924), 869.

[141] Haller: *Compt. rend.*, **112** (1891), 1490; **113** (1892), 22.

Colorless crystals; melt with decomposition at 244°; slightly soluble in alcohol; insoluble in water; hydrochloric acid solutions are stable; aqueous alkalies decompose the substance into antimonic acid and camphor.

E. Stibonium Compounds.

Tetramethylstibonium hydroxide: $(CH_3)_4SbOH$. An aqueous solution of tetramethylstibonium iodide is shaken with fresh silver oxide, filtered, and evaporated *in vacuo*.[143]

White, crystalline, deliquescent solid; very soluble in water and alcohol. This substance is strongly alkaline; it absorbs carbon dioxide from the air, liberates ammonia from ammonium salts, precipitates metallic hydroxides from solutions of their salts, redissolves zinc hydroxide when in excess and dissolves sulfur. The conductivity of a solution of a gram-molecule in 16 l. of water is 166.[144]

Tetramethylstibonium Salts:

Iodide: $(CH_3)_4SbI$. A mixture of trimethylstibine and methyl iodide gradually solidifies; the crystals are recrystallized from water.[145]

White plates; soluble in 3.3 parts of water at 23°; soluble in alcohol but not in ether. Concentrated hydrochloric or sulfuric acid liberates hydrogen iodide, and chlorine or bromine liberates iodine.

Chloride. A solution of the stibonium iodide or hydroxide in hydrochloric acid is evaporated; or the iodide is treated with a hot solution of mercuric chloride, and the filtrate from the mercuric iodide is evaporated.[146]

Deliquescent, white crystals; soluble in water and alcohol, but insoluble in ether. Forms a double salt with platinic chloride:

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[142] Ref. 107, p. 35.

[143a] Landolt: *Ann.*, 78 (1851), 93.

[b] *Ibid.*, 84 (1852), 50.

[144] Bredig: *Zeit. physik. Chem.*, 13 (1894), 301.

[145] Ref. 143a, p. 95; Ref. 143b, p. 44.

[146] Ref. 143a, p. 96; Ref. 143b, p. 59.

$2[(CH_3)_4SbCl] \cdot PtCl_4$; yellow crystals; insoluble in water, alcohol and ether; soluble in hydrochloric acid.[147]

Bromide. The stibonium iodide is treated with a hot solution of mercuric bromide; the filtrate from the mercuric iodide is evaporated to crystallization.[148]

Colorless crystals; soluble in water and alcohol but insoluble in ether.

Nitrate. An aqueous solution of the iodide is treated with silver nitrate, filtered and evaporated.[149] Small needles; very soluble in water, but difficultly soluble in alcohol and ether.

Sulfate: $[(CH_3)_4Sb]_2SO_4 \cdot 5H_2O$. Prepared by the same method as the nitrate.[150] Colorless crystals which are soluble in water and alcohol, but insoluble in ether. When treated with the calculated amount of sulfuric acid, an acid sulfate is obtained as transparent plates which are very soluble in water, difficultly soluble in alcohol, and insoluble in ether.

Bicarbonate. An aqueous solution of the base is saturated with carbon dioxide and evaporated.[151] Small needles.

Sulfide. An aqueous solution of the hydroxide is saturated with hydrogen sulfide, and after the addition of an equivalent quantity of the stibonium base, the solution is evaporated.[152] Amorphous powder; soluble in water and alcohol but insoluble in ether.

Acetate. Obtained as a sirup by treating the iodide with silver acetate.[153]

Oxalate. Crystalline solid, prepared by treating the hydroxide with oxalic acid and evaporating the solution.[154]

Tetraethylstibonium hydroxide: $(C_2H_5)_4SbOH$. The stibonium iodide is treated in aqueous or alcoholic solution with fresh silver oxide; the filtrate from the silver iodide is evaporated on a water bath and then in a desiccator over sulfuric acid.[155]

The double salt, $(C_2H_5)_4SbI \cdot HgI_2$, is treated in the presence of alcohol with silver oxide; evaporation of the filtrate yields the hydroxide.[156]

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[147] Ref. 143b, p. 61.
[148] Ref. 143b, p. 58.
[149] Ref. 143a, p. 95; Ref. 143b, p. 66.
[150] Ref. 143a, p. 94; Ref. 143b, p. 62.
[151] Ref. 143a, p. 95; Ref. 143b, p. 67.
[152] Ref. 143b, p. 53.
[153] Ref. 143b, p. 68.
[154] Ref. 143b, p. 69.
[155] Löwig: *Ann.*, **97** (1856), 327.

Practically colorless, viscous oil; soluble in all proportions in water and alcohol; insoluble in ether. This substance is a very strong alkali; it liberates ammonia from its salts, precipitates the hydroxides of the heavy metals from solutions of their salts; and when in excess, it redissolves the hydroxides of tin and aluminum.

Tetraethylstibonium Salts:

Iodide: $(C_2H_5)_4SbI \cdot 1\frac{1}{2}H_2O$. Equal volumes of triethylstibine and ethyliodide are heated in a sealed tube at 100° with 6-8 volumes of water. The clear solution is evaporated on a water-bath.[157]

Large, transparent, hexagonal crystals; 19 parts dissolve in 100 parts of water at 20°; very soluble in alcohol, insoluble in ether. Reacts with mercuric chloride, in aqueous solution, forming a white, crystalline, insoluble double salt, $(C_2H_5)_4SbI \cdot 3HgI_2$, and tetraethylstibonium chloride. If the iodide is treated with freshly precipitated mercuric iodide, a double salt, $2(C_2H_5)_4SbI \cdot 3HgI_2$, is obtained.[158]

Another double salt with mercuric iodide, $(C_2H_5)_4SbI \cdot HgI_2$, may be obtained in a crystalline condition by heating 10 g. of antimony amalgam with 25 g. of ethyl iodide in a sealed tube in boiling aniline.[159]

Tetraethylstibonium halides form crystalline double salts with bismuth halides:[160] $3(C_2H_5)_4SbI \cdot 2BiI_3$, red; $3(C_2H_5)_4SbBr \cdot 2BiBr_3$, yellow; $3(C_2H_5)_4SbI \cdot 2BiBr_3$.

A yellow double salt, $(C_2H_5)_4SbI \cdot CHI_3$, separates when an alcoholic solution of tetraethylstibonium iodide and iodoform is cooled after refluxing.[161] When boiled with water, the substance decomposes into its constituents.

Chloride: $(C_2H_5)_4SbCl$. Obtained from the mother liquor from the double salt, $2(C_2H_5)_4SbI \cdot 3HgI_2$, which forms when the stibonium iodide is treated with mercuric chloride.[162]

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[156] Partheil and Mannheim: *Arch. der Pharm.,* **238** (1900), 174; *J. Chem. Soc. Abst.,* **78** (1900), I, 479.

[157] Ref. 155, p. 323.

[158a] Ref. 155, p. 326.

[b] Löwig: *J. prakt. Chem.,* [1] **64** (1855), 420.

[159] Partheil and Mannheim: *Arch. der Pharm.,* **238** (1900), 174; *J. Chem. Soc. Abst.,* **78** (1900), I, 479.

[160] Jörgensen: *J. prakt. Chem.,* [2] **3** (1871), 340, 342.

[161] Steinkopf and Schwen: *Ber.,* **54B** (1921), 2969.

[162] Ref. 155, p. 324.

It may be prepared more readily by neutralizing the stibonium hydroxide with hydrochloric acid and evaporating the solution to dryness.[163]

Small, hygroscopic needles; soluble in water and alcohol. It forms double salts with mercuric, auric, and platinic chlorides:[164]

$(C_2H_5)_4SbCl \cdot 4HgCl_2$, colorless crystals, m.p. 141-142°;
$(C_2H_5)_4SbCl \cdot AuCl_3\frac{1}{2}H_2O$, yellow needles, m.p. 178°;
$[(C_2H_5)_4SbCl]_2PtCl_4$, yellowish red crystals.

Bromide: $(C_2H_5)_4SbBr$. A solution of the hydroxide is neutralized with hydrobromic acid and evaporated.[165] Colorless needles; soluble in water and alcohol.

Sulfate. Small crystals obtained by treating the iodide with silver sulfate and evaporating the filtrate from the silver iodide.[166]

Nitrate. Long, colorless needles prepared in the same manner as the sulfate.

Formate. Hot solutions of lead formate and the stibonium iodide are mixed, and the lead iodide is filtered out at once; the filtrate deposits colorless needles upon cooling. This salt is difficultly soluble in water but soluble in alcohol; it turns yellow in the air.

Acetate. Prepared in the same manner as the formate; it is more soluble in water.

Oxalate. A solution of the hydroxide is neutralized with oxalic acid and evaporated to crystallization.

Tartrate. Prepared in the same manner as the oxalate, but evaporation of the solution yields a sirup which crystallizes slowly.

Hydrosulfide. A solution of the hydroxide is saturated with hydrogen sulfide and evaporated; yellow oil which is soluble in water and alcohol.

Succinate. Prepared from the hydroxide and succinic acid; the sirup which remains when the solution is evaporated does not crystallize.[167]

Methyl-triethylstibonium hydroxide: $(CH_3)(C_2H_5)_3SbOH$.

The stibonium sulfate is treated in aqueous solution with barium hydroxide, and the filtrate from the barium sulfate is evaporated in the absence of carbon dioxide.[168]

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[163] Ref. 158b, p. 422.

[164] Partheil and Mannheim: *Arch. der Pharm.*, **238** (1900), 174; *J. Chem. Soc. Abst.*, **78** (1900), I, 479.

[165] Ref. 155, p. 327.

[166] Ref. 155, p. 328.

[167] Ref. 158b, p. 420.

[168] Friedländer: *J. prakt. Chem.*, **70** (1857), 456.

Viscous, slightly yellow oil which, like the other stibonium hydroxides, is a strong alkali.

Methyltriethylstibonium Salts:

Iodide. Triethylstibine, suspended in warm water, is treated with methyl iodide in an atmosphere of carbon dioxide until the odor of the stibine disappears. The clear solution is evaporated to dryness.[169] Colorless, hexagonal prisms; soluble in 2 parts of water at 20°, and alcohol; insoluble in ether.

Chloride. A hot aqueous solution of the iodide is treated with a hot solution of mercuric chloride; a yellow, insoluble double salt of the stibonium iodide and mercuric iodide separates, and the filtrate yields the stibonium chloride when evaporated. Or, an aqueous solution of the hydroxide or the carbonate may be treated with hydrochloric acid and evaporated.[170]

Sulfate. A hot, aqueous solution of the iodide is treated with silver sulfate, filtered and evaporated; or an aqueous solution of the hydroxide or carbonate is treated with sulfuric acid and evaporated.[171] Colorless, deliquescent crystals; m.p. 100°.

Nitrate. By double decomposition between the iodide and silver nitrate, or the sulfate and barium nitrate; the filtered solution is evaporated to crystallization.[172] Colorless, deliquescent needles.

Carbonate. A resinous mass obtained by treating the sulfate with barium carbonate and evaporating the filtrate.[172]

Formate. A hot, aqueous solution of the iodide is treated with lead formate, filtered and cooled. Fine, colorless needles which are only slightly soluble in cold water or alcohol.[173]

Acetate. Colorless needles obtained by the same method as the carbonate, using barium acetate.[174]

Butyrate. Colorless crystals; the sulfate is treated with barium butyrate, and the filtered solution is evaporated.[172]

Oxalates. Neutral and acid oxalates are obtained as colorless needles by treating oxalic acid with 2 and 1 equivalents of the stibonium hydroxide respectively and evaporating the solution.[175]

Tartrate. A solution of tartaric acid is treated with 2 equivalents of the stibonium hydroxide and evaporated; the resulting sirup does not crystallize.[175]

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[169] Ref. 168, p. 450.
[170] Ref. 168, p. 453, 455.
[171] Ref. 168, p. 457.
[172] Ref. 168, p. 458.
[173] Ref. 168, p. 459.
[174] Ref. 168, p. 460.
[175] Ref. 168, p. 461.

Hydrosulfide. An aqueous solution of the hydroxide is saturated with hydrogen sulfide and evaporated; the residue is an oil.[176]

Titrapropylstibonium hydroxide: $(C_3H_7)_4SbOH$.

Antimony amalgam and propyl iodide react to form a yellow, crystalline double salt $(C_3H_7)_4SbI \cdot HgI_2$, m.p. 103.5°, which is converted into tetrapropylstibonium hydroxide,[156] very hygroscopic needles, by means of silver oxide. The stibonium chloride, a hygroscopic crystalline substance, forms double salts with mercuric, auric and platinic chlorides; $(C_3H_7)_4SbCl \cdot HgCl_2$ needles, m.p. 120-121°; $(C_3H_7)_4SbCl \cdot AuCl_3$, yellow needles, m.p. 98°; $[(C_3H_7)_4SbCl]_2PtCl_4$, yellow-red octahedra, m.p. 133°. The stibonium picrate is a yellow, crystalline solid, m.p. 67.5°.

Phenyl-trimethylstibonium iodide: $C_6H_5(CH_3)_3SbI$. Formed quantitatively when phenyl-dimethylstibine and excess methyl iodide are refluxed for a short time. Fine, white needles; readily soluble in water and alcohol, difficultly soluble in ether or petroleum ether.[177]

Phenyl-ethyl-dimethylstibonium iodide: $C_6H_5(C_2H_5)(CH_3)_2SbI$.

Phenyl-dimethylstibine and excess ethyl iodide are heated at 100° in a sealed tube for 5 hours.[177] White needles; readily soluble in water and alcohol, but insoluble in ether.

Phenyl-methyl-diethylstibonium iodide: $C_6H_5(CH_3)(C_2H_5)_2SbI$.

Phenyl-diethylstibine and methyl iodide combine rather slowly, but a quantitative yield of the stibonium compound is obtained by heating for 2 hours at 100°.[178] White needles.

[176] Ref. 168, p. 462.
[177] Ref. 94, p. 1760.
[178] Ref. 94, p. 1761.

Chapter 9.

Antimonyl Compounds.

A. Antimonyl Tartrates.

With a few exceptions the antimonyl tartrates have been prepared either by refluxing an aqueous solution of an acid salt of tartaric acid with antimony trioxide, or by double decomposition between barium antimonyl tartrate and the sulfate of a base. Consequently, an example of each of these methods will be given, and in the subsequent enumeration of the individual compounds, the preparation will be stated merely as Method A or B.

Method A: Potassium antimonyl tartrate—A solution of 5 g. of potassium bitartrate in 50 cc. of water is refluxed with 4 g. of freshly prepared antimony trioxide for 2 hours. The filtrate from the excess antimony oxide deposits crystalline tartar emetic upon cooling, and a second crop of crystals may be obtained by evaporating the filtrate, total yield 7 g.

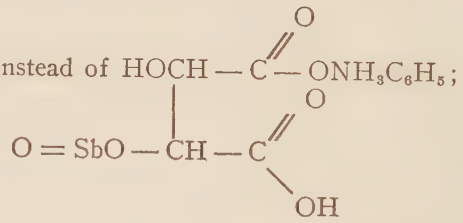
The antimony oxide is best prepared by diluting a hydrochloric acid solution of the commercial oxide with water and neutralizing with ammonia; the washed precipitate is dried at room temperature in a vacuum. If the commercial material is employed, the reaction is considerably slower. The removal of the excess oxide from the reaction mixture is greatly facilitated by the addition of a small quantity of vegetable carbon.

In preparing other antimonyl tartrates by this method, the bitartrate solution is prepared by adding one molecular proportion of a mono acidic base or half a molecular proportion of a diacidic base to a solution of tartaric acid. Frequently it is necessary to concentrate the solution of the antimonyl compound before crystallization takes place; sometimes the product is precipitated by the addition of alcohol after evaporation; in some cases the solution must be completely evaporated and the residual sirup solidified either by treatment with alcohol or by permitting it to stand for several days. In general, the solutions may be evaporated on a water bath, but in some instances the application of heat must be avoided. The products are recrystallized either from water or alcohol-water mixtures.

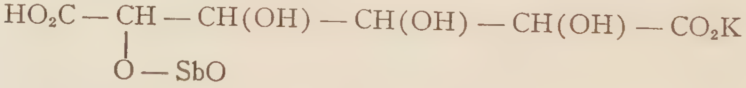
Method B: A hot, aqueous solution of the sulfate of a base is treated with an equivalent quantity of finely powdered barium antimonyl tartrate; about 100 cc. of water is used per 10 g. of the latter compound. The barium salt does not dissolve to any great extent, and the suspension is stirred until the filtered sample no longer gives a test for sulfate ions—usually 2 hours suffices. The reaction product is isolated from the filtrate from the barium sulfate either by cooling or evaporating to crystallization as in A.

Instead of complete structural formulæ for the individual antimonyl compounds, semi-empirical formulæ will be given, e.g., aniline antimonyl tartrate will be written as

$C_6H_5NH_3(SbO)C_4H_4O_6$ instead of



the group $[(SbO)C_4H_4O_6]$ will be used to represent the antimonyl tartrate ion. Similarly, potassium antimonyl mucate will be written as $K(SbO)C_6H_8O_8$ instead of



$$HO_2C-\underset{\displaystyle O-SbO}{\underset{|}{CH}}-CH(OH)-CH(OH)-CH(OH)-CO_2K$$

Potassium antimonyl tartrate (tartar emetic): $K(SbO)C_4H_4O_6 \cdot \frac{1}{2}H_2O$

Method A: colorless, transparent crystals; effloresce in the air; insoluble in alcohol; solubility in water—8.3 g./100 cc. at 25° and 33 g./100 cc. at 100°; density 2.5888;[1] sp. gr. at 17.5° of a 1% solution 1.007, of a 5% solution 1.035;[2] pH of a 1% solution is approximately 5; the molecular rotation of a solution of a gram-mol. per liter of water is 548° [3]—Baudran[4] found that the specific rotation of solutions of tartar emetic is slightly variable and depends upon the nature of the potassium bitartrate from which it is prepared; the molecular conductivity of a solution of a gram-mol per 8 l. of water is 70.58. The water of crystallization is removed very readily at 100-110°; at higher temperatures water of constitution is expelled[5] leaving a solid which absorbs moisture very rapidly in the air.

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[1] Buignet: *Jahrb. Fort. Chem.* (1861), 15.

[2] Streit: *Zeit. analyt. Chem.*, **22** (1883), 110.

[3a] Hädrich: *Zeit. physik. Chem.*, **12** (1893), 494.

[b] Grossman: *Zeit. physik. Chem.*, **54** (1896), 412.

[4] Baudran: *Ann. Chim. Phys.*, [7] **19** (1900), 536.

Aqueous solutions of tartar emetic are free from antimony ions,[6] but they hydrolyze quite readily and deposit antimony oxide. Concentrated solutions are quite stable, but as the dilution is increased hydrolysis takes place;[7] a 1.6% solution deposits 3.5% of its antimony during a period of 14 months.[8] The growth of fungi in these solutions may be avoided by adding tartaric and hydrochloric acids;[8] the tartaric acid must be added in order to prevent the precipitation of antimony oxide by the hydrochloric acid. Although neutral salts affect aqueous solutions of tartar emetic very little, alkaline salts, acids, or alkalies cause decomposition; the extent to which this occurs depends upon the temperature, concentration, and nature of the reagent added, but the antimony is never completely precipitated.[9] This decomposition is accompanied by a decrease in the optical rotation.

In addition to its use in chemotherapy, tartar emetic has been employed very extensively as a fixing agent for tannic acid in mordanting processes and to some extent in analytical work for the standardization of iodine solutions.[10]

Sodium antimonyl tartrate: $Na(SbO)C_4H_4O_6 \cdot \frac{1}{2}H_2O$

Method A: white crystals; readily soluble in water, insoluble in alcohol.[11]

Lithium antimonyl tartrate: $Li(SbO)C_4H_4O_6 \cdot 2\frac{1}{2}H_2O$

Method A: obtained as a difficultly crystallizable sirup by

[5a] Dumas and Piria: *Ann.*, **44** (1842), 85.
[b] Hale: *J. Amer. Chem. Soc.*, **24** (1902), 828.
[6] Kahlenberg: *Zeit. physik. Chem.*, **17** (1895), 605.
[7a] Hädrich: *Zeit. physik Chem.*, **12** (1893), 494.
[b] Grossman: *Zeit. physik. Chem.*, **54** (1896), 412.
[8] Gruener: *Amer. J. Sci.*, [3] **46** (1893), 206.
[9a] Clarke and Stallo: *Amer. Chem. J.*, **2** (1880-1), 319.
[b] Long: *Amer. J. Sci. and Arts.*, [3] **38** (1889), 264; **40** (1890), 275; *J. Amer. Chem. Soc.*, **17** (1895), 87.
[c] Long and Sauer: *Chem. News*, **63** (1891), 269.
[10a] Ref. 5b.
[b] Metzel: *Zeit. anorg. Chem.*, **48** (1906), 160.
[c] Lutz: *Zeit. anorg. Chem.*, **49** (1906), 338.
[11a] Ref. 5a.
[b] Plimmer: *Proc. Royal Soc. London*, [B] **80** (1908), 11.

evaporation of the solution. When a fragment of ammonium antimonyl tartrate is added, the sirup solidifies and may then be recrystallized from alcohol-water mixtures. Colorless octahedra; 180 g. dissolve in 100 cc. of water at 18°.[12]

Rubidium antimonyl tartrate.

Method A: isomorphous with the potassium salt.[13]

Cæsium antimonyl tartrate: $Cs[(SbO)C_4H_4O_6]\frac{1}{2}H_2O$

Method A, or by the action of cæsium chloride on silver antimonyl tartrate; may be precipitated as a crystalline solid from an aqueous solution by the addition of alcohol. Soluble in 3.5 parts of water at 20°.[14]

Calcium antimonyl tartrate: $Ca[(SbO)C_4H_4O_6]_2 \cdot 6\frac{1}{2}H_2O$

Method A: may be recrystallized from water.[15]

Strontium antimonyl tartrate: $Sr[(SbO)C_4H_4O_6]_2$. Method A.[16]

Barium antimonyl tartrate: $Ba[(SbO)C_4H_4O_6]_2 \cdot 3H_2O$

Crystallizes when hot solutions of tartar emetic and barium chloride are mixed. Colorless, hexagonal plates containing 3 molecules of water[17] instead of 2½;[18] insoluble in cold water.

Silver antimonyl tartrate: $Ag(SbO)C_4H_4O_6 \cdot H_2O$

Separates in white, granular crystals when solutions of tartar emetic and silver nitrate are mixed.[19] Solubility in 100 cc. of water: 0.2 g. at 15°, 1 g. at 100°.

Ammonium antimonyl tartrate: $NH_4(SbO)(C_4H_4O_6)$

Method A: colorless crystals, practically insoluble in alcohol. Three hydrates are known: (a) ½ a molecule of water of crystallization;[20] (b) $1H_2O$;[21] (c) $1\frac{1}{2}H_2O$ large flattened prisms—66 g. dissolve in 100 cc. of water at 18°.[22]

[12a] Fargher and Gray: *J. Pharm. and Exper. Therap.*, **18** (1921), 348.
[b] Brahmachari: *Indian J. Medical Research,* **11** (1923), 196.
[c] Christiansen and Norton: *J. Amer. Chem. Soc.*, **47** (1925), 877, prefer Method B for preparation of this compound.

[13] Grandeau: *Ann. Chim. Phys.*, [3] **67** (1863), 231.

[14] Costeanu: *Bull. soc. sci. acad. Roumaine,* **8** (1923), 215.

[15] Ref. 12b, p. 197.

[16] Ref. 12b, p. 198.

[17] Ref. 12a, p. 347.

[18] Hale: *J. Amer. Chem. Soc.*, **24** (1902), 828.

[19] Ref. 12b, p. 199.

[20a] Ref. 5b.
[b] Brahmachari: *Indian J. Medical Research,* **10** (1922), 497.

[21] Berlin: *Ann.*, **64** (1847), 359.

[22] Ref. 12a, p. 348.

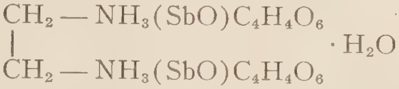
Tetramethylammonium antimonyl tartrate:
$(CH_3)_4N(SbO)C_4H_4O_6$

From silver antimonyl tartrate and tetramethylammonium iodide.[23]

Butylamine antimonyl tartrate: $C_4H_9NH_3(SbO)C_4H_4O_6 \cdot 2H_2O$

Method B: evaporation of the filtrate from the barium sulfate leaves a sirup from which prisms separate gradually. Recrystallize from alcohol. Large, rectangular plates; m.p. 40°—the dehydrated material melts at 155°; 238 g. dissolve in 100 cc. of water 18°.[24]

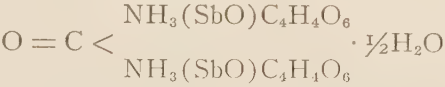
Ethylenediamine antimonyl tartrate:



$$\begin{array}{l} CH_2 - NH_3(SbO)C_4H_4O_6 \\ | \\ CH_2 - NH_3(SbO)C_4H_4O_6 \end{array} \cdot H_2O$$

Method A: colorless prisms, slightly soluble in alcohol; 4 g. dissolve in 100 cc. of water at 18°; darkens at 280° but does not melt even at 300°.[25]

Urea antimonyl tartrate:



$$O = C < \begin{array}{l} NH_3(SbO)C_4H_4O_6 \\ NH_3(SbO)C_4H_4O_6 \end{array} \cdot \tfrac{1}{2}H_2O$$

Method A: the filtrate from the antimony oxide is evaporated to a sirup which gradually crystallizes.[26] It is rather unusual that both amino groups of urea should enter into salt formation.

Aniline antimonyl tartrate: $C_6H_5NH_3(SbO)C_4H_4O_6$

Method A,[27] or B:[28] obtained as monohydrated, colorless needles by crystallization from water at 15° and as an anhydrous substance by crystallization at 35°. Very soluble in water and alcohol; insoluble in acetone; the aqueous solution is dextrorotatory.

Benzylamine antimonyl tartrate:
$C_6H_5CH_2NH_3(SbO)C_4H_4O_6 \cdot \tfrac{1}{2}H_2O$

Method B: colorless plates; fairly soluble in water; pH of a 1% solution is 5.[29]

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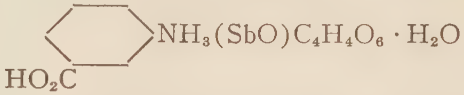
[23] Clarke: *Ber.,* **15** (1882), 1540.
[24] Ref. 12a, p. 349.
[25] Fargher and Gray: *J. Pharm. and Exper. Therap.,* **18** (1921), 348.
[26] Ref. 20b, p. 496.
[27a] Yvon: *Compt. rend.,* **150** (1910), 283; *J. Pharm. Chim.,* [7] **1** (1910), 233, 281.
[b] Ref. 12a, p. 350.
[c] Ref. 20b, p. 498.
[28] Clarke: *Ber.,* **15** (1882), 1540.
[29] Christiansen and Norton: *J. Amer. Chem. Soc.,* **47** (1925), 876.

Phenylhydrazine antimonyl tartrate:

$$C_6H_5NH \cdot NH_3(SbO)C_4H_4O_6$$

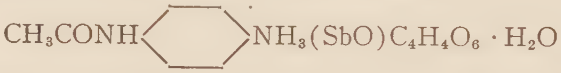
Method B: slightly yellow crystals; readily soluble in water; pH of a 1% solution is 5.[29]

m-Carboxyaniline antimonyl tartrate:



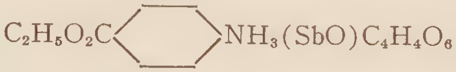
Method B: stout, slightly purple colored needles; pH of a 1% solution is 2.6.[29]

Acetyl-p-phenylenediamine antimonyl tartrate:



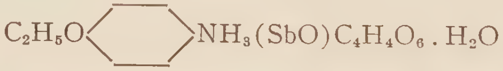
Method B: slightly brown, minute crystals; pH of a 1% solution is 2.[29]

p-Carboethoxy-aniline antimonyl tartrate:



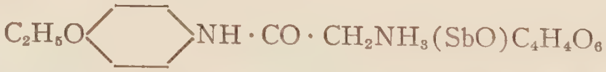
Method A: well defined crystals; slightly soluble in water.[30]

p-Phenetidine antimonyl tartrate:



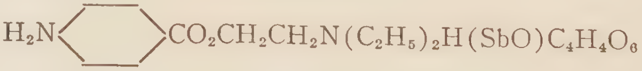
Method A: fine needles; m.p. 148°—the anhydrous material melts at 245°; solubility in water 8.5 g./100 cc. at 18°.[31]

p-Phenetidinyl-acetamido-antimonyl tartrate (phenocoll antimonyl tartrate):



Method A: the sirup obtained by evaporation of the solution crystallizes when agitated.[30]

p-Amino-benzoyldiethylamino-ethanol mono-antimonyl tartrate: (Novocaine mono-antimonyl tartrate):



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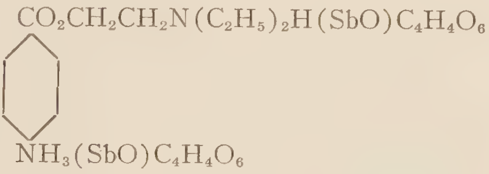
[30] Brahmachari: *Indian J. Med. Res.*, 11 (1923), 406.
[31] Ref. 12a, p. 350.

An aqueous solution of novocaine hydrochloride is shaken with silver antimonyl tartrate in the absence of sunlight for 6 days; the gel which is obtained by evaporation of the filtrate from the silver chloride in a vacuum desiccator solidifies when treated with alcohol. White hygroscopic powder; very soluble in alcohol.[32]

p-Amino-benzoyldiethylamino-ethanol di-antimonyl tartrate: (Novocaine-di-antimonyl tartrate):



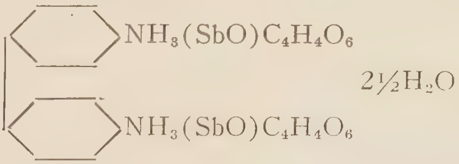
Method A: precipitates as a crystalline solid when alcohol is added to the evaporated solution. Very hygroscopic and soluble in water; decomposes in the air if moist.[32]

Diethyl-amino-propylcinnamate antimonyl tartrate:
(Apothesine antimonyl tartrate):

$$C_6H_5CH = CHCO_2CH_2CH_2CH_2N(C_2H_5)_2H(SbO)C_4H_4O_6$$

Apothesine hydrochloride, in aqueous solution, is shaken for 48 hours with silver antimonyl chloride; the filtrate from the silver chloride, when evaporated in a vacuum desiccator, yields a gel which solidifies when treated with alcohol. Very hygroscopic and soluble in water.[33]

Benzidine antimonyl tartrate:



Method B: colorless needles; does not melt below 260°; pH of a 1% solution is 4.6.[34]

3,6-Diamino-10-methylacridinium-antimonyl tartrate (acriflavine antimonyl tartrate):

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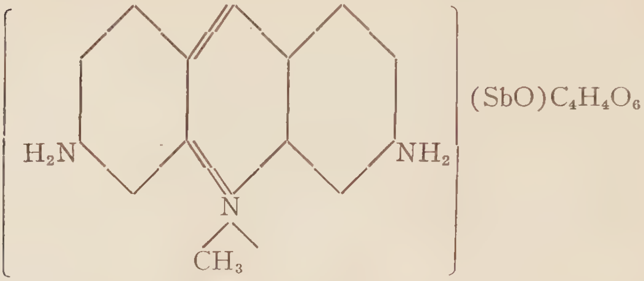
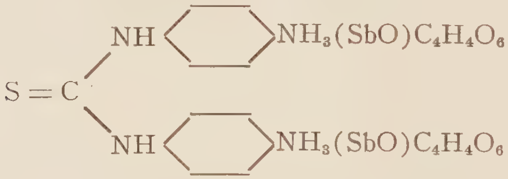
[32] Ref. 30, p. 407.
[33] Ref. 30, p. 408.
[34] Christiansen and Norton: *J. Amer. Chem. Soc.*, **47** (1925), 876.



3,6-Diamino-10-methylacridinium chloride is refluxed in pyridine solution with silver antimonyl tartrate; the precipitate is washed with pyridine, alcohol, and water. The product is lighter colored than acriflavine and is only slightly soluble in water.[35]

p,p′-Diamino-diphenylthiourea-di-antimonyl tartrate:



A cold suspension of powdered barium antimonyl tartrate is treated with the calculated quantity of cold, dilute sulfuric acid, and the cold filtrate from the barium sulfate is neutralized by adding the calculated quantity of powdered p,p′-diamino-diphenyl thiourea. After clarification, the solution is evaporated and poured into alcohol; the product precipitates at once.[34] Slightly pink colored powder; does not melt below 310°; slightly soluble in water.

Quinine antimonyl tartrate: $(C_{20}H_{25}O_2N_2)(SbO)C_4H_4O_6 \cdot H_2O$

Method B:[36, 37] If an aqueous solution of quinine and tartaric acid is boiled with antimony oxide, the quinine is converted into quinotoxine, and an oil, probably quinotoxine antimonyl tartrate, is obtained which does not crystallize readily.[37] Slender needles; dissolve very slowly in water—1.01 g./100 cc. at 18°.

Quinidine antimonyl tartrate:

$$(C_{20}H_{25}O_2N_2)(SbO)C_4H_4O_6 \cdot 4H_2O$$

Method A or B:[38] crystallizes when solutions of tartar emetic and a soluble salt of quinidine are mixed.[39] Slender needles; solubility in water—0.31 g./100 cc. at 18°.

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[35] Ref. 30, p. 409.

[36] Clarke: *Ber.*, **15** (1882), 1540.

[37] Ref. 12a, p. 350.

[38] Ref. 12a, p. 351.

Hydroquinine antimonyl tartrate:
$(C_{20}H_{27}O_2N_2)(SbO)C_4H_4O_6 . 5H_2O$

Method B: crystalline; m.p. 201°; solubility in water—2.24 g./100 cc. at 18°.[40]

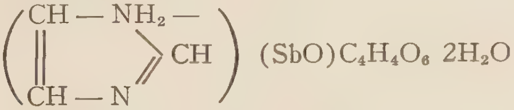
Cinchonine antimonyl tartrate: $(C_{19}H_{23}ON_2)(SbO)C_4H_4O_6$

Method A or B: three hydrates are known containing ½,[38] 1½,[41] and 2½ [42] molecules of water respectively. Solubility of the lowest hydrate in water—2.96 g./100 cc. at 18°.

Cinchonidine antimonyl tartrate:
$(C_{19}H_{23}ON_2)(SbO)C_4H_4O_6 \cdot 2\frac{1}{2}H_2O$

Method B: large, rectangular plates; m.p. 192°; solubility in water—1.37 g./100 cc. at 18°.[40]

Glyoxaline antimonyl tartrate:



Method A: flat prisms; does not melt at 300°; slightly soluble in organic solvents; solubility in water—46.7 g./100 cc. at 18°.[43]

Atropine antimonyl tartrate: Method B: very soluble in water.[36]

Narcotine antimonyl tartrate: $(C_{22}H_{24}O_7N)(SbO)C_4H_4O_6$

Method A: needle-like crystals.[44]

Ethyl antimonyl tartrate: $C_2H_5(SbO)C_4H_4O_6$

(a) Ethyl tartrate is heated with antimony oxide in a sealed tube at 150°; no experimental details are given.[45]

(b) Silver antimonyl tartrate (dried at 105°) is refluxed with a solution of ethyl iodide in absolute alcohol; the insoluble matter is extracted with water and the extract is evaporated at a low temperature.[46] White powder; dissolves in water, forming a solution which is distinctly acid to litmus.

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[39] Hesse: *Ann.,* **146** (1868), 369.
[40] Ref. 12a, p. 352.
[41] Traube: *Z. Kr.,* **29** (1897), 600.
[42] Traube: *Jahrb. f. Mineral.,* 11 Beilageband, 623.
[43] Ref. 12a, p. 349.
[44] Ref. 12b, p. 202.
[45] Thomson and Cushny: *Proc. Roy. Soc. London,* [B] **82** (1910), 252.
[46] Ref. 12b, p. 199.

iso-Propyl antimonyl tartrate: $(CH_3)_2CH(SbO)C_4H_4O_6$

Anhydrous silver antimonyl tartrate is refluxed with a solution of iso-propyl iodide in absolute iso-propyl alcohol; the insoluble matter is extracted with water at room temperature, and the extract is evaporated in a vacuum desiccator over sodium hydroxide. The sirup which is obtained solidifies when it is treated with alcohol.[34] Colorless powder; dissolves very readily in water, forming a solution which is slightly acid to Congo Red.

Trimethylsulfonium antimonyl tartrate:

$(CH_3)_3S(SbO)C_4H_4O_6\frac{1}{2}H_2O$

Method A: white crystals from alcohol.[47]

B. Antimonyl Derivatives of Other Aliphatic Hydroxy Acids.

1. *Potassium antimonyl glycollate.* An aqueous solution of glycollic acid containing 0.5 of an equivalent of potassium hydroxide is refluxed with antimony trioxide. The product is isolated as a double salt with potassium glycollate[48]—$2[K(SbO)(C_2H_3O_3)_2] \cdot KO_2CCH_2OH \cdot H_2O$.

2. *Antimonyl citrates:*[49] *Potassium salt*—

$K_3(SbO)(C_6H_6O_7)_2 \cdot 2H_2O$

An aqueous solution of primary potassium citrate is refluxed with antimony trioxide; recrystallize from dilute alcohol. Small, colorless needles; readily soluble in water; the aqueous solution is strongly acid to litmus.

Sodium salt—$Na_3(SbO)(C_6H_6O_7)_2H_2O$. Prepared in same way as the potassium salt. Minute needles.

Ammonium salt—$(NH_4)_3(SbO)(C_6H_6O_7)_2 \cdot H_2O$. Colorless prisms.

3. *Antimonyl mucates: Potassium salt*—$K(SbO)C_6H_8O_8 \cdot 4H_2O$. After an aqueous solution of acid potassium mucate has been boiled with antimony trioxide, a double salt, $2K(SbO)C_6H_8O_8 \cdot KC_6H_9O_8 \cdot 6H_2O$, is obtained as a white crystalline powder which, when recrystallized several times, yields the simple antimonyl compound.[50]

Ammonium salt: $NH_4(SbO)C_6H_8O_8 \cdot 3H_2O$. Obtained as a double salt, $2NH_4(SbO)C_6H_8O_8 \cdot NH_4C_6H_9O_8 \cdot 7H_2O$, by the method used for the potassium salt. Repeated recrystallization yields the simple salt. White, crystalline powder; sparingly soluble in cold water; fairly soluble in hot water.[51]

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[47] Strömholm: *Ber.*, 33 (1900), 828.

[48] Jordis and Meyer: *Zeit. angew. Chem.*, 17 (1904), 169.

[b] Ger. Pat. 263,455.

[49] Henderson and Prentice: *J. Chem. Soc.*, 67 (1895), 1030.

[50] Ref. 49, p. 1037.

Sodium salt: $Na(SbO)C_6H_8O_8 \cdot 3H_2O$. Obtained directly from the reaction mixture; there is no evidence of double salt formation in this case. Crystalline powder; slightly soluble in cold water, readily soluble in hot water.[51, 52]

4. *Antimonyl malates.* When the primary malates are refluxed in aqueous solution with antimony oxide, the reaction products are isolated as double salts from which the simple derivatives cannot be readily obtained. Different investigators appear to have secured different products.

Potassium salt: $2Sb_2O(C_4H_4O_5K)_4 \cdot Sb_2O(C_4H_5O_5)_4 \cdot 7H_2O$ [53]

Ammonium salt:

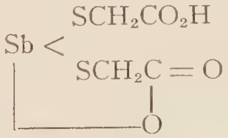
$2Sb_2O(C_4H_4O_5NH_4)_4 \cdot Sb_2O(C_4H_5O_5)_4 \cdot 20H_2O$ [53]

$NH_4(SbO)C_1H_4O_5 \cdot NH_4C_4H_5O_5 \cdot 5H_2O$ [54]

Sodium salt: $Na(SbO)C_4H_4O_5 \cdot Na(SbO)C_4H_5O_5 \cdot xH_2O$ [54]

C. Derivatives of Thioglycollic Acid.

Antimony thioglycollic acid:



$$Sb{<}\begin{matrix} SCH_2CO_2H \\ SCH_2C{=}O \\ \quad\;\; | \\ \quad\;\; O \end{matrix}$$

(a) Thioglycollic acid (3 mol.) is added to antimony trichloride dissolved in dilute hydrochloric acid;[55] ether may be used as a reaction medium.[56]

(b) A concentrated, aqueous solution of thioglycollic acid is refluxed with antimony trioxide.[55]

White crystals; readily soluble in glacial acetic acid and hot water; solubility in water at 25°—1.43 g./100 cc. Decomposed by excess potassium hydroxide.

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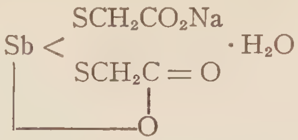
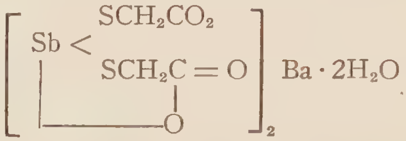
[51] Henderson and Barr: *J. Chem. Soc.*, **69** (1896), 1454.
[52] Klein: *Compt. rend.*, **97** (1883), 1437.
[53] Ref. 51, p. 1452.
[54] Ref. 12b, p. 207.
[55] Klason and Carlson: *Ber.*, **39** (1906), 737.
[56] Holmberg: *Zeit. anorg. Chem.*, **56** (1907-8), 385.

Sodium salt:



Colorless, prismatic crystals; very soluble in water.[57]

Barium salt:



Colorless, glistening needles; readily soluble in hot water; difficultly soluble in cold water.[57]

The potassium salt has been secured only as a sirup.

Ethyl antimony thioglycollate: $Sb(SCH_2CO_2C_2H_5)_3$

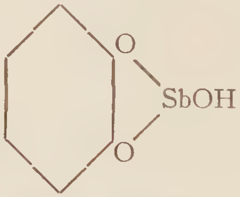
Ethyl thioglycollate (20 g.) is treated with 0.5 g. portions ot antimony trioxide with vigorous shaking till a slight excess of the latter has been added; the oil is separated from the water which is eliminated during the reaction and from the excess antimony oxide. On long standing clusters of glittering, prismatic crystals separate.[58]

Antimony thioglycollamide: $Sb(SCH_2CONH_2)_3$

An absolute alcoholic solution of ethyl antimony thioglycollate is treated with ammonia; the amide separates as a viscous mass.[59] Colorless or slightly reddish, semi-resinous substance; very soluble in water; slightly soluble in alcohol; decomposed by aqueous alkalies with the deposition of antimony oxide.

D. Derivatives of Polyhydric Phenols.

Antimonyl catechol:



An aqueous solution of catechol, which has been saturated with sodium chloride, is treated on a water bath with a warm solution of antimony chloride in sodium chloride. The product crystallizes gradually upon cooling.[60]

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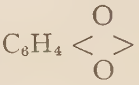
[57] Ramberg: *Ber.*, **39** (1906), 1357.
[58] Rowntree and Abel: *J. Pharm. and Exper. Therap.*, **2** (1910), 109.
[59] Ref. 58, p. 110.

Prismatic crystals; insoluble in water, alcohol, ether, and chloroform; dissolves in halogen acids, forming the halides; decomposed by nitric and sulfuric acid; yields antimony sulfide when treated with hydrogen sulfide. Decomposes when heated in a sealed tube with acetic anhydride forming diacetylcatechol.

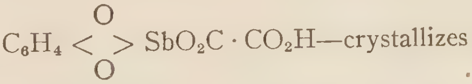


Chloride: $C_6H_4 < \overset{O}{\underset{O}{}} > SbCl$.-crystallizes gradually from an alcoholic solution of catechol and antimony trichloride[61] or from a hydrochloric acid solution of antimony trichloride and catechol.[62] Crystalline; insoluble in ordinary solvents; hydrolyzed by water to form the hydroxy compound.

Bromide—prepared in the same way as the chloride.

Iodide—precipitates when a solution of antimony oxide in an aqueous solution of hydrogen iodide and potassium iodide is treated with catechol.

Fluoride—separates as a crystalline solid when aqueous solutions of catechol and antimony fluoride are mixed.



Oxalate: $C_6H_4 < \overset{O}{\underset{O}{}} > SbO_2C \cdot CO_2H$—crystallizes when a hot solution of the chloride in aqueous hydrochloric acid is treated with a hot, saturated solution of potassium acid oxalate; microscopic needles, insoluble in water.

Acetate—the antimonyl compound is treated with acetic anhydride and acetyl chloride in the presence of glacial acetic acid.

Catechol derivatives substituted with carboxylic, sulfonic, arsonic or other acid group yield antimony compounds when heated with antimonious acid in water. The alkali salts of the products form stable neutral solutions.[63]

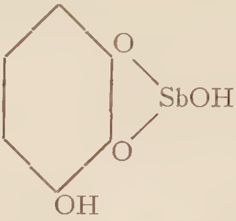
[60a] Causse: *Bull. soc. chim.*, [3] **8** (1892), 245.
[b] Causse: *Ann. Chim. Phys.*, [7] **14** (1898), 539.

[61] Ref. 60b, p. 541.

[62] Causse: *Compt. rend.*, **125** (1897), 954.

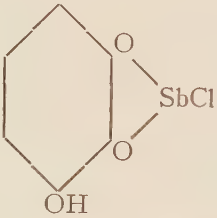
[63] Brit. Pat. 213,285.

Antimonyl-pyrogallol:



Crystallizes slowly when an aqueous solution pyrogallol is added to a solution of tartar emetic.[64] Colorless crystals; stable in the air; insoluble in water and organic solvents; soluble in alkalies and in halogen acids; decomposed by acetyl chloride forming triacetyl pyrogallol.

Chloride:



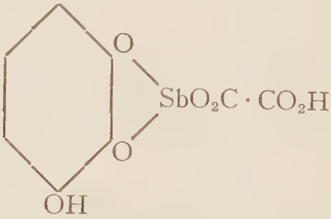
Formed by the action of antimony trichloride on pyrogallol in aqueous or alcoholic solution, or by treating the antimonyl compound with hydrochloric acid.[65] Colorless crystals.

Bromide—crystallizes when an aqueous solution of pyrogallol and potassium bromide is added to a hydrobromic acid solution of antimony bromide containing potassium bromide.

Iodide—pyrogallol is treated with antimony iodide in the presence of hydrogen iodide and potassium iodide.

Fluoride—a solution of antimony fluoride is treated with a solution of pyrogallol.

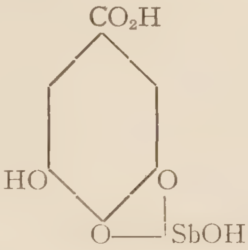
Oxalate:



[64a] Rosing: *Compt. rend.*, **46** (1858), 1140.
[b] Causse: *Compt. rend.*, **115** (1892), 507.
[c] Ref. 60b, p. 551.
[65] Ref. 60b, p. 552.

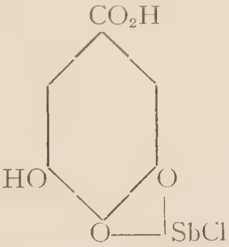
The antimonyl compound is treated in hydrochloric acid solution with potassium acid oxalate; colorless needles; insoluble in water.

Antimonyl gallic acid:



A warm solution of tartar emetic, or a sodium chloride solution of antimony trichloride is treated with gallic acid. In the latter case, it is necessary to heat the crude product with water in order to hydrolyze the chloride which is also present.[66]

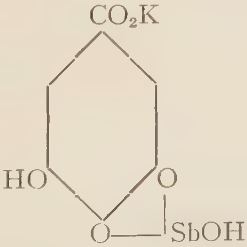
Chloride:



The antimonyl compound is treated with hydrochloric acid; microscopic needles.

Bromide—obtained in a similar manner; colorless crystals.

Potassium antimonyl gallate:



A solution of the free acid in hot, aqueous potassium bicarbonate yields microscopic crystals of the potassium salt when cooled.

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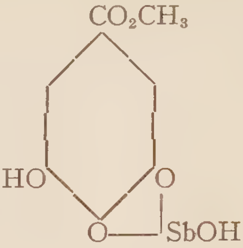
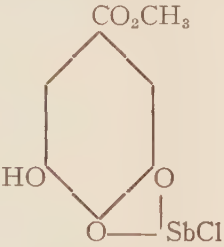
[66] Ref. 60b, p. 560.

Methyl antimonyl gallate:



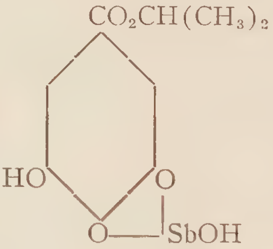
Prepared by the action of antimony trichloride on methyl gallate in methyl alcohol solution; the material which gradually separates is contaminated with some of the corresponding chloride and must be boiled with water in order to hydrolyze the latter.[67] Small, colorless crystals; insoluble in water.

Chloride:



Colorless crystals obtained by dissolving the antimonyl compound in warm hydrochloric acid.

iso-Propyl antimonyl gallate:



A hot, aqueous solution of iso-propyl gallate is added to a hot solution of sodium antimonyl tartrate; the white precipitate is dried *in vacuo* over caustic soda.[68] Colorless powder; insoluble in water or sodium carbonate; readily soluble in sodium hydroxide.

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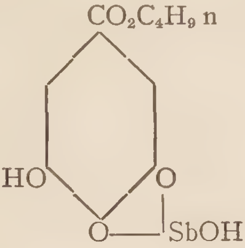
[67] Ref. 60b, p. 557.

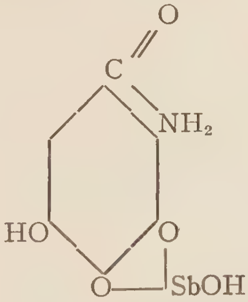
[68] Private communication from W. G. Christiansen.

n-Butyl antimonyl gallate:



Hot, aqueous solutions of n-butyl gallate and sodium antimonyl gallate are mixed; the colorless precipitate is dried *in vacuo* over caustic soda.[68] Colorless powder; insoluble in water or sodium carbonate; readily soluble in sodium hydroxide.

Antimonyl gallamide:



Hot, aqueous solutions of gallamide and sodium antimonyl gallate are mixed; the white precipitate which gradually separates is dried and then extracted by boiling with water. The residue is dried *in vacuo* over caustic soda.[68] Slightly cream colored powder; readily soluble in sodium hydroxide.

Antimonyl tannic acid.[69] When solutions of tannic acid and tartar emetic are mixed, the nature of the product depends upon the proportion of reagents used and the experimental conditions; three compounds have been obtained as white powders, which are stable in the air:

In cold solutions with excess tartar emetic → $C_{14}H_9(SbO)O_9$

In dilute solutions with no excess of tartar emetic → $(C_{14}H_9O_9)_2SbOH$

At 80-90° with excess tartar emetic → $(C_{14}H_8(SbO)O_9)_2SbOH$

The structural formulæ of these substances have not been determined, but in view of the nature of the antimonials which may be

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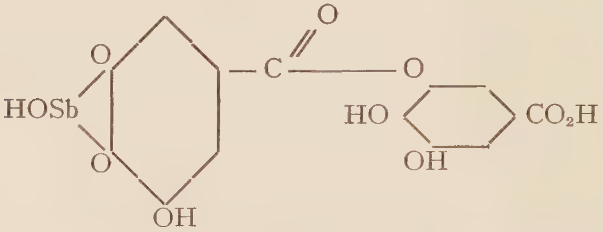
[69a] Ljubavin: *J. Russ. Phys. Chem. Soc.*, **33** (1901), 680.

[b] Sanin: *Zeit. Farb. Ind.*, **9** (1910), 2.

obtained from the simple polyphenols, it seems that the first of the above compounds may be:



These are the substances which are formed during the fixation of tannic acid during the mordanting of cloth.

E. Esters of Antimonious Acid[70] — R_3O_3Sb

Aliphatic esters: Antimony trioxide and an aliphatic alcohol are refluxed in a flask to which a Soxhlet tube, containing anhydrous copper sulfate, and a condenser are attached. After 15 hours the liquid is separated from the excess antimony oxide and fractionated under diminished pressure.

			b.p.
Methyl antimonite:	colorless	liquid;	65°
Ethyl "	"	"	115-120°
Propyl "	yellow	"	143° at 30^{mm}
iso Butyl "	"	"	144° at 30^{mm}
Amyl "			170° at 30^{mm}
iso Amyl "			163° at 30^{mm}

Aromatic esters: These may be prepared either by refluxing in a Soxhlet apparatus as in the case of the aliphatic compounds, or by refluxing the phenol with antimony trioxide and calcium turnings.

		m.p.	b.p. at 30^{mm}
Phenyl antimonite:	light brown crystals;	13°	250°
o-Tolyl "	dark brown crystals;	16°	352°
m-Tolyl "	yellow liquid;		300°
p-Tolyl "	dark brown crystals;	14°	345°

All the esters are readily soluble in alcohol, ether, chloroform, and benzene; water hydrolyzes them immediately.

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[70] Mackey: *J. Chem. Soc.*, **95** (1909), 604.

Chapter 10.

Analysis.

A. Determination of Antimony in C-Sb Compounds.

(a) Aryl stibinous oxides and triaryl stibines which contain an amino group attached to the benzene ring may be titrated with iodine in dilute, slightly acid solution.[1]

(b)[2] A mixture of about 0.2 g. of the substance, 0.2 g. of sodium chloride and 3 g. of sodium bisulfate is treated in a Kjeldahl flask with a mixture of 1.5 cc. of nitric acid (sp. gr. 1.49) and 10 cc. of concentrated sulfuric acid and heated for an hour; at first a small flame is used, but during the last 30 minutes a much hotter one is applied. After cooling, 1 g. of ammonium sulfate is added, and the flask is again heated for ½ an hour to remove the nitric acid. After dilution to about 300 cc. and addition of 20 cc. of 5N-hydrochloric acid, 1 g. of potassium bromide and an aqueous solution of sulfur dioxide are added in order to reduce the antimonic acid.[3] The excess sulfur dioxide is removed by boiling; tartaric acid is added after the solution has cooled, and sodium bicarbonate is added till the solution is neutral. The antimony trioxide is titrated with N/10 iodine solution.

(c)[4] 0.2 gram of the finely powdered substance is intimately mixed in a dry 300 cc. flask with 1 g. of finely powdered potassium permanganate, and 10 cc. of 50 per cent sulfuric acid are added quickly whilst shaking the flask. A second gram of permanganate is then introduced, followed by 10 cc. of concentrated sulfuric acid in small portions.

After the mixture has been allowed to stand for a few minutes, 10 cc. of water are added, and the mixture then boiled for half an hour under a simple reflux condenser formed by a wide tube with a bulb to rest on the neck of the flask. Hydrogen peroxide is then added in slight excess, followed by 30 cc. of water, and the solution again boiled until a drop of a dilute solution of potassium permanganate gives a faint permanent pink color. This is discharged by a drop of a dilute solution of oxalic acid, the solution is cooled, diluted to 150 cc., 2.5 g. of potassium iodide added, the flask stoppered and allowed to stand for an hour before titration with sodium thiosulfate N/10. A yellow color often persists after all the iodine has disappeared, so that starch must be used as indicator. A control should be carried out simultaneously with the antimony compound omitted and the result corrected accordingly.

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[1] Schmidt: *Ann.*, **421** (1920), 244.

[2a] Ref. 1, p. 245.

[b] A special method is used for arsenic-antimony compounds; Schmidt: *Ber.*, **57B** (1924), 1148.

[3] Rohmer: *Ber.*, **34** (1901), 1565.

[4] Fargher and Gray: *J. Pharm. and Exper. Therap.*, **18** (1921), 356.

(d)[5] 0.2 g. of substance, dissolved if possible in 10 cc. of water by the addition of alkali, is treated with 1 g. of potassium permanganate and 10 cc. of concentrated sulfuric acid. After heating for a time, the mixture is decolorized by boiling with 10-15 cc. of hydrochloric acid, and diluted with 50 cc. of water and 75 cc. of hydrochloric acid. The antimony is reduced in the cooled solution by shaking for 3 minutes with 5 g. of potassium iodide. After diluting with a further 124 cc. of water, the solution is titrated with N/10 thiosulfate, using starch as indicator. If a blank be subtracted, each cc. of thiosulfate then equals 0.006 g. of Sb or 3%.

(e) The powdered substance (0.2-0.3 g.) is mixed in a nickel crucible with 10-15 g. of a mixture of sodium carbonate and sodium peroxide (1:1) and gradually heated till the mass is fused. An aqueous solution of the resulting mixture is acidified with hydrochloric acid, and the antimony is precipitated from the boiling solution with hydrogen sulfide. The antimony sulfide may be collected and dried in a stream of carbon dioxide or converted into the tetraoxide by treatment with fuming nitric acid (cf. Section B).

(f)[6] A small boat containing the substance, mixed with sodalime and lime, is placed in a hard glass tube (11 mm. diam.), and granular lime is introduced until there is an 8 cm. layer at each end of the boat. The tube is heated gradually, starting at the ends and working toward the center; at first a slow stream of air is passed through the tube but oxygen is used during the last part of the ignition. The combustion should be so regulated that there is no visible burning of the organic material. The contents of the tube are dissolved in water and after acidification with hydrochloric acid the antimony is precipitated with hydrogen sulfide. The trisulfide is oxidized with fuming nitric acid and the antimony is weighed as Sb_2O_4 (cf. Section B).

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[5] Macallum: *J. Soc. Chem. Ind.*, **42** (1923), 470T.

[6] Michaelis and Genzken: *Ann.*, **242** (1887), 168.

B. Determination of Antimony in C-O-Sb Compounds.

(a) The antimony in antimonyl compounds of the tartar emetic type may be determined very easily by direct titration with iodine, provided the remainder of the molecule does not contain any group which will reduce iodine.

Half a gram of the substance is dissolved in 50 cc. of water, and after the addition of 1 g. of tartaric acid and 25 cc. of saturated sodium bicarbonate solution, the solution is titrated with 0.1 N iodine, using starch as an indicator. The end point is preceded by a fading violet color.[7]

(b) The C-O-Sb compounds all yield antimony sulfide very readily when treated with hydrogen sulfide in acid solution. In view of the facts that all antimonyl compounds can not be titrated with iodine and that in all cases the end point is preceded by the fading violet color, it is frequently preferable to determine the antimony gravimetrically as the sulfide. The method of Vortmann and Metzel may be employed:[8] 0.2 g. of substance is dissolved in 12 cc. of concentrated hydrochloric acid and 38 cc. of water in a 200 cc. Erlenmeyer flask. It is heated to boiling, and the hot solution subjected to the action of hydrogen sulfide gas. The Erlenmeyer flask containing the solution is placed in a dish of boiling water and the water in the latter is kept boiling during the precipitation. It is advisable to introduce the hydrogen sulfide gas quite rapidly at first, but towards the end a slow stream is sufficient. The antimony sulfide as it comes down is yellow at first, but as the precipitation proceeds, it becomes redder; gradually it becomes heavier and denser, assumes a crystalline form and becomes darker, and finally black in color. The transformation into the crystalline form is hastened by shaking the flask. At first, while the precipitate is of a yellowish color, there is no need of shaking the flask, but later on it is very desirable to do so. The shaking, however, should not be too violent, as otherwise some of the precipitate is likely to adhere to the upper portions of the flask and escape the transformation. The duration of the whole process amounts to from 30 to 35 minutes. Finally a heavy, dense, crystalline precipitate of antimony trisulfide is obtained which settles well and permits a rapid filtration. The solution is diluted with an equal volume of water, which is allowed to flow around the walls of the flask in order to wash down any adhering sulfide. The dilution almost always causes the formation of a slight yellow turbidity. The reason for this is that a little of the antimony is held in solution by the strong acid and as the solution is diluted this is caused to precipitate by the dissolved hydrogen sulfide. The flask is, therefore, once more shaken, placed in the vessel of boiling water and more hydrogen sulfide is introduced. In two or three minutes the solution above the precipitate will become clear. It is filtered through a Gooch crucible, washed with water to remove the acid, then with alcohol, and placed in the drying oven.

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[7] Dunstan and Boole: *Pharm. J. Trans.,* [3] 19 (1888), 385.
Hale: *J. Amer. Chem. Soc.,* 24 (1902), 831.

[8] Treadwell-Hall: "Analytical Chemistry," Vol. II, Wiley, 5th ed., p. 221.

In some instances the precipitate does not readily pass into the black, crystalline modification, and it is advisable to adopt the method of Henz[9] and dry the sulfide, after collection on a Gooch crucible, in a current of dry carbon dioxide, first at 100-130° and then at 280-300°.

Instead of weighing the precipitated sulfide, the latter may be converted into antimony tetroxide.[10]

C. Determination of Antimony in Biological Material.

(a) One hundred grams of finely divided tissues in a porcelain casserole in a water bath is brought to the consistency of thin gruel with distilled water and treated with 100 g. of hydrochloric acid. Small quantities of potassium chlorate are added till the solid matter disappears and a clear yellow liquid is obtained. After heating till the odor of chlorine disappears, the liquid is filtered and made up to 250 cc. An aliquot portion is digested with sulfuric acid, and the acid residue is diluted, neutralized with a slight excess of potassium hydroxide, slightly acidified with tartaric acid, and treated with sodium bicarbonate solution. The antimony is determined by titration with 0.1 N iodine.[11]

(b) After destruction of the organic matter with potassium chlorate and hydrochloric acid, the insoluble matter is filtered out and washed with hot water containing hydrochloric acid. The filtrate is concentrated on a water bath to remove some of the acid, diluted with water and partially neutralized with ammonia. The cold solution is saturated with hydrogen sulfide and gradually heated to boiling without interrupting the stream of hydrogen sulfide. The antimony sulfide is filtered and washed, and the filter paper containing the precipitate is heated on a water bath with hydrochloric acid until the solid has dissolved. After filtering, the solution is diluted, partially neutralized and reprecipitated with hydrogen sulfide. The antimony sulfide is collected on a Gooch crucible and dried in a stream of carbon dioxide first at 130° and then at 280-300°.[12]

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[9] Ref. 8, p. 218.

[10] Ref. 8, p. 223.

[11] Norton and Koch: *J. Amer. Chem. Soc.*, **27** (1905), 1249.

The results with feces are high, and the twice precipitated antimony sulfide must be dissolved in ammonium sulfide, filtered and reprecipitated with hydrochloric acid.

Several other methods have been used which will not be described here.[13]

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[12] Brunner: *Arch. Exp. Path. and Pharm.*, **68** (1912), 189.

[13a] Schidrowitz and Goldsborough: *Analyst.*, **36** (1911), 101.

[b] Brahmachari, Das, and Sen: *Indian J. Medical Research*, **11** (1923), 417.

Appendix.

After the manuscript of this monograph went to press, several papers dealing with antimonials appeared. The purpose of this appendix is to indicate the nature of the studies reported in these papers.

Trimethylstibine. While studying the reactions between trimethylstibine and platinic and palladous chlorides, Morgan and Yarsley[1] devised an apparatus in which the stibine may be generated from trimethylstibinic bromide by distillation with granulated zinc and converted into platinum and palladium derivatives without any danger of explosion. When chloroplatinic acid is treated with trimethylstibine, reduction occurs giving rise to trimethylstibinic chloride and platinous chloride. The latter reacts with more trimethylstibine forming one or two additive compounds depending on the nature of the solvent. In aqueous solution, only tetrakistrimethylstibine-platinous platinochloride, $[Pt, 4(CH_3)_3Sb]PtCl_4$, forms; in alcoholic solution, this compound and bistrimethylstibinedichloroplatinum, $2(CH_3)_3Sb \cdot PtCl_2$, are both formed. These substances have been converted into the following compounds: tetrakistrimethylstibineplatinouschloride, $[Pt, 4(CH_3)_3Sb]Cl_2$; tetrakistrimethylstibineplatinous platinichloride, $[Pt, 4(CH_3)_3Sb]PtCl_6$; tetrakistrimethylstibineplatinous palladochloride, $[Pt, 4(CH_3)_3Sb]PdCl_4$.

Trimethylstibine and palladous chloride interact to form bistrimethylstibinedichloropalladium, $2(CH_3)_3Sb \cdot PdCl_2$, which may be converted into tetrakistrimethylstibinepalladous chloride, $[Pd, 4(CH_3)_3Sb]Cl_2$. The latter may be converted into trimethylstibinedichloropalladium hydrochloride, $[(CH_3)_3Sb \cdot PdCl_3]H$.

Tri-α-naphthylstibine. Matsumiya[2] finds that α-naphthylmagnesium bromide reacts with amorphous antimony trisulfide, as well as with antimony trichloride, to form tri-α-naphthylstibine; the crystalline modification of the trisulfide is practically inactive. The m.p. is given

$$6C_{10}H_7MgBr + Sb_2S_3 \rightarrow 2(C_{10}H_7)_3Sb + 3MgBr_2 + 3MgS$$

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[1] Morgan and Yarsley: *J. Chem. Soc.*, **127** (1925), 184.

[2] Matsumiya: *Mem. of the College of Sci., Kyoto Imp. Univ.*, [A], **8** (1925), 12.

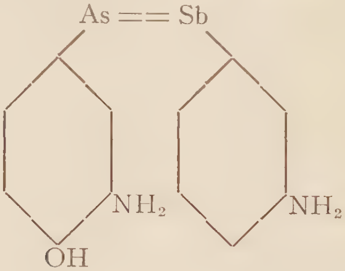
as 216-217°.[3] Attempts to prepare di-α-naphthylstibinous chloride by using one molecule or less of the Grignard reagent per mol. of antimony chloride failed; the tertiary stibine was the only organic product. The stibinic chloride and bromine, as obtained by treating tri-α-naphthylstibine in benzene or carbon bisulfide solution with chlorine and bromine respectively, were found to melt at 256° and 232° respectively.[4]

Matsumiya read his paper on April 6, 1924, and must have studied these compounds contemporaneously with Challenger and Pritchard.

Tri-α-naphthylstibinic oxide: $(C_{10}H_7)_3SbO$

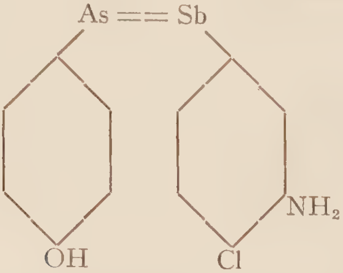
The stibinic chloride or bromide is refluxed with alcoholic potash and benzene for 20 hours, and the reaction product is recrystallized from carbon bisulfide-benzene. The resulting crystals contain a molecule of benzene which is expelled by heating; the oxide is an amorphous powder,[2] m.p. 219-220°.

3,3′-Diamino-4-hydroxyarseno-stibinobenzene:



3-Amino-4-hydroxyphenylarsine is condensed with 3-aminophenylstibinous oxide.[5]

4-Hydroxy-3′-amino-4′-chloroarseno-stibinobenzene:



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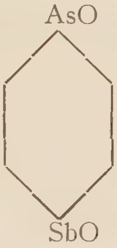
[3] Challenger and Pritchard: *J. Chem. Soc.*, **125** (1924), 869, report the m.p. as 218°.

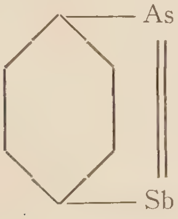
[4] Challenger and Pritchard (Ref. 3) report: chloride, m.p. 260°; bromide, m.p. 229°.

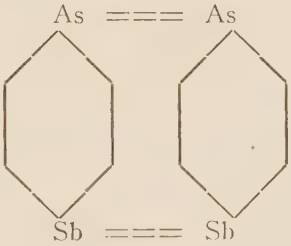
[5] Ger. Pat. 396,697.

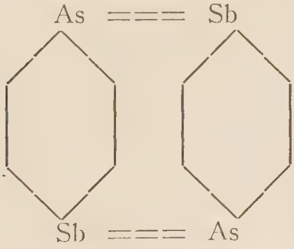
4-Hydroxyphenylarsine is condensed with 3-amino-4-chlorophenylstibinous oxide.[5]

Reduction products of 4-arsonophenylstibinic acid.

When 4-arsonophenylstibinic acid is reduced with sulphur dioxide and hydriodic acid, 4-arsinophenylstibinous oxide,  , is produced. The latter, when reduced with phosphorous acid and hydriodic acid, yields a yellow solid[6] which might be represented by either of the following formulæ:[6]







If the arsono stibinic acid is reduced with sodium hydrosulfite, only dark brown products are obtained.

Reduction product of 2-hydroxy-5-arsonophenyl-stibinic acid.

When this acid is reduced with stannous chloride and hydriodic acid, an orange yellow solid is obtained.[6]

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[6] Ger. Pat. 397,151.

Arsenic-antimony compounds.

3-amino-4-hydroxyphenylarsine reacts with tartar emetic in aqueous, alkaline solution to form dark brown arsenic antimony compounds.[7]

4-Hydroxyphenylarsine reacts with an hydrated antimony trioxide to form an arsenic antimony compound.[7]

Antimonyl pyrogallol. Feigl[8] utilizes the formation of antimonyl pyrogallol in dilute hydrochloric acid solution for the determination of antimony. A distinct test can be obtained using 5 cc. of a tartaric acid solution which contains 4.6 mg. Sb per liter. It can also be used in separating antimony and arsenic; the latter is determined in the filtrate from the pyrogallol precipitate. Example: found Sb 9.41% and As 18.72%, calculated Sb 9.10% and As 18.50%.

Double salts of antimony halides with aromatic compounds.[9]

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[7] Ger. Pat. 397,275.

[8] Feigl: *Mikrochem.,* **1** (1923), 74; *Zeit. analyt. Chem.,* **64** (1924), 41.

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